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THE AUTONOMIC NERVOUS SYSTEM



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THE AUTONOMIC NERVOUS SYSTEM

ANATOMY, PHYSIOLOGY, AND SURGICAL APPLICATION

BY

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DEDICATED TO

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Former Chief of the Neurosurgical Service

and to

ARTHUR W. ALLEN

Former Chief of the Peripheral Vascular Clinic
Present Chief of the East Surgical Service
of the Massachusetts General Hospital

FOREWORD

WE are thrust into the world by smooth muscle, which is under control of the autonomic nervous system. From moment to moment we are dependent for our conscious existence on the moderate contraction of blood vessels, routinely kept in that state by autonomic impulses. Most of the complicated processes of digestion, from the initial outpouring of saliva to the final riddance of waste, require the participation of autonomic nerves. Any vigorous exercise in which we may engage depends upon coöperation of the autonomic government of appropriate effectors; thus throughout eons of past time the physical struggle for existence has been made possible by that government. And that government, furthermore, normally preserves, even to the stage of senescent decline, the stable states of the fluid matrix of the body that are required for ready response to every call for action.

Despite the essential rôle which the autonomic system plays in such fundamental services as continuance of the race, maintenance of effective relations with our surroundings, and provision for our sustenance and our fitness for effort, relatively little attention has been given, until recent times, to its natural modes of operating and to the muscles and glands through which it operates. For decades eminent physiological investigators engaged in ingenious experimenting on striated muscle, but paid slight regard to the functioning of smooth muscle. And efforts to explain glandular secretion were slighter still. Thus neglect of the agents of autonomic nerves accompanied meager attention to the structural and functional characteristics of the nerves themselves.

Only since the comprehensive studies of Gaskell and Langley were begun, about a half-century ago, has much insight into the organization of the elements of the "involuntary" or "vegetative" nervous system been gained. Still more recently have the physiological values of the system to the organism as a whole been

somewhat clarified, and its connections with the central nervous axis partially traced. At present interest centers on the implications of the fresh discovery that autonomic impulses are transmitted to muscles and glands by chemical substances, adrenaline and acetylcholine, which are the directly effective deputies of the nerve impulses.

Understanding of the highly significant rôle played by the autonomic system in the functioning of the body has opened new vistas. The ways have been revealed in which pain, cold, various emotional states and other conditions which excite autonomic discharges can induce or participate in pathological processes. Thereby morbid phenomena which have long been regarded as mysterious have received reasonable explanation.

Practical effects of advances in knowledge of the anatomy, physiology, and pathology of the autonomic system have been seen in both pharmacotherapy and in surgery, especially in the latter. The opportunities of progressing beyond the boundaries of familiar surgery seemed to have been coming to an end. In being subjected to surgical skill, however, as in being subjected to comprehensive scientific study, the autonomic system suffered neglect. Here was a chance for pioneering, and it was taken. Leriche in France, Adson, and White and Smithwick in the United States have made impressive advances in applying surgical technique to the treatment of pathological states resulting from abnormal autonomic activity. White's earlier volume on the anatomy, physiology, and surgical treatment of the autonomic system marked an important step forward in summarizing both scientific information and its practical significance. In the present volume White and Smithwick have admirably gathered the latest knowledge of the structure and functions of the system, and reported from their own extensive experience and from the experience of others the methods by which surgery can be applied to the cure or mitigation of disorders of autonomic origin.

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PREFACE

In preparing a second edition of this monograph the most difficult problem has been to incorporate the great mass of important data which has appeared in the past six years without unduly lengthening it. In order to keep the book within practical bounds it has been necessary to eliminate many of the older references, as well as some of the case histories and illustrations included in the first edition.

The majority of our patients have been admitted to beds on the Neurosurgical Service and the Peripheral Vascular and Cardiac Clinics of the Massachusetts General Hospital. For permission to utilize this invaluable material we wish to express our particular thanks to Dr. W. J. Mixter, Dr. L. S. McKittrick, Dr. P. D. White, and their associates. We have also drawn freely on the laboratory and clinical departments of the Harvard Medical School and its associated hospitals for technical advice and additional clinical material. We wish to express our indebtedness and gratitude to the members of these departments who have helped us. Similar acknowledgments are due to Dr. N. E. Freeman (now at the University of Pennsylvania), Dr. J. V. Meigs, and Dr. W. P. Chapman for their generous collaboration.

In the preparation of this text we have had the advantage of the criticism and advice of Dr. Donal Sheehan, Professor of Anatomy at New York University, in the historical chapter; Professor W. B. Cannon, Dr. Arturo Rosenblueth, and Dr. R. S. Morison of the Harvard Medical School in the chapters on physiology and anatomy; Dr. John Homans in the section on pain in the extremities; Dr. Stanley Cobb in the portions relating to the central nervous system; and Drs. I. H. Page, J. H. Means, and R. S. Palmer in the chapter on hypertension. In the other clinical chapters invaluable assistance has been rendered by members of the hospital staff who are especially interested in these fields. It is impossible to thank everyone who has helped us individually,

and we trust that they will not regard this omission as a lack of appreciation.

The successful preparation of this book has been made possible by the devoted and intelligent work of our secretaries, Miss Lucy Allen and Miss Mildred Rogers; of the hospital librarian, Miss Caroline Williams, who has located countless obscure references; and of Miss Muriel McLatchie, who has made the drawings.

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INTRODUCTION

The first edition of this monograph, which appeared in 1935, was written at a time when surgeons were just beginning to understand the effect of interrupting the cardiovascular and other visceral nerves. The subject had to be approached with the realization that much of what was set down would require revision. As predicted, understanding of function and the therapeutic possibilities of surgical intervention have both advanced at such speed that now, at the end of six years, the book must be rewritten and considerably enlarged. This second edition, like the first, is written for students of neurology as well as for those who are concerned in the practical application of neurophysiology to disordered visceral function and intractable pain. In order to make it of the greatest practical value to the clinical investigator, as well as to the general practitioner and the surgeon, we have endeavored to gather into one volume the fundamental contributions of the anatomist, the physiologist, and the pharmacologist, as well as those of the internist and the neurosurgeon. The increasing opportunities to modify abnormal visceral activity and sensation by neurosurgical measures require a fundamental approach to the concepts of visceral innervation. In no field of modern medicine has information derived from animal experimentation played a more vital rôle in clinical progress. The current literature is so vast that we have been able to mention only the more important articles, but the reader who is interested in any particular field can obtain a very complete bibliography by referring to these publications. In the past many clinical articles have been written in a spirit of over-enthusiasm so common to pioneer work and with inadequate follow-up studies. Failure to obtain the results to be expected from reading descriptions of new forms of surgical treatment has been a discouraging experi-

ence of all surgeons who have worked in this field. In writing the following chapters, therefore, it is our intention to rely only on experiences which have been extensively verified and to discuss the bad as well as the good results observed at the Massachusetts General Hospital. *In this way we believe that fairly* definite statements can be made and defended on many of the therapeutic problems which are discussed in the following chapters. A few still remain in the experimental stage and are presented as such.

An unusual opportunity has been presented at the Massachusetts General Hospital for investigation in this field. This has been facilitated by the close liaison between the general and neurosurgical services with the neurological, cardiac, and peripheral vascular clinics. An additional advantage has been the spirit of coöperation shown by our patients, nearly all of whom have returned to the hospital at frequent intervals for postoperative tests and observations. The interchange of ideas and advice obtained from Professor Cannon and other departments of the Harvard Medical School has been a constant stimulus. Before several of the perplexing problems concerning peripheral circulation and cardiac pain could be settled, it was necessary to take them back to the experimental laboratory and then, with a more physiological insight derived from this source, to start afresh on the clinical attack. The problem of modifying the activity of the visceral nervous system in man still remains a challenge to both the physiologist and the surgeon.

Several monographs on the surgery of the autonomic nervous system have appeared, the earliest being those by Brüning and Stahl in 1924 and by Hesse of Leningrad in 1930. Both are written in German. Recent advances in physiology and neurosurgical knowledge have been so rapid that these books are now out of date. In England a good short monograph has been published by Gask and Ross (1934) with a second edition in 1937, but this deals with only a limited part of the field of autonomic neurosurgery. In this country W. K. Livingston (1935) has written another, which is particularly interesting because of the author's wide experience with traumatic arthritis, causalgia, and amputation stump neuralgia. In addition to these texts, a valuable symposium on *The Vegetative Nervous System* was published by the Association for Research in Nervous and Mental

Disease in 1930, and many reviews of special subjects, such as Hinsey's (1939) and Sheehan's (1941) on physiology, and annual reports on progress by White in *Surgery*, Smithwick in *The New England Journal of Medicine*, and Livingston in *Confinia Neurologica* serve to make the more valuable current contributions accessible to the average physician.

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PART I

Chapter II

THE HISTORICAL DEVELOPMENT OF KNOWLEDGE OF THE INVOLUNTARY NERVOUS SYSTEM

The earliest recorded reference to the visceral nervous system was made by Galen * in the second century. He gave the first account of the paravertebral sympathetic chains with their superior and inferior cervical and semilunar ganglia, but made the mistake of describing the sympathetic and vagal trunks as one structure originating within the cranium. This gave rise to an error which persisted for fifteen hundred years. Galen was the first to note that the denervated heart maintained its beat, as he observed that hearts removed in animal sacrifices continued to beat in the hands of the priests. Following these observations of the great Greek physician, little progress was made through the ensuing fourteen centuries until the time of Vesalius (1543), who made dissections and diagrams of the sympathetic ganglionated trunks and some of the important peripheral plexuses. Like Galen, Vesalius (Fig. 1) depicted a combined vago-sympathetic trunk arising from the brain stem. Stephanos (1545) and later Eustachius (1563) were the first to distinguish the two separate nerves, but in the Eustachian plate the sympathetic trunks arise from the abducens nerves. The copper plates of Eustachius' dissections made in 1552 were never published during his lifetime, but remained in the papal library for a hundred and sixty-two years. Finally Pope Clement XI presented the plates to his physician, Lancisius, who published them in 1714 (Fig. 2).

In the seventeenth century Willis (1664) published a remarkably clear account of the ganglionated chains and their connections with the intercostal nerves. He described the cardiac

* See *De usu partium corporis humani* (1550) and Daremberg's translation (1854).

branches and stated that the great mesenteric plexus, placed in the midst of others like a sun, sent its nerve fibers like rays in all directions; hence it came to be called the solar plexus. He considered that its function was to place the heart and viscera in connection with the brain so that they should act in harmony. The modern nomenclature of the cranial nerves originated with Willis. In addition he gave an accurate description of the vagus or "wandering nerve," with a true understanding of its apparent union with the cervical sympathetic in some of the lower mammals and its separate course in man. He even noted the branch given off to the aortic arch, "so it may react to changes in the pulse." According to Sheehan (1936), who describes the conception of the autonomic nervous system at the end of the seventeenth century, the "intercostal" (sympathetic) and "wandering" (vagus) nerves, though clearly separated anatomically, remained physiologically one system, possessing a double function. On account of its numerous intercommunications, it was looked on as the *modus operandi* by which "sympathy" could be brought about between different parts of the body. When one stops to remember that this concept was based almost entirely on anatomical observations, it constitutes a most remarkable hypothesis.

In 1732 the Danish anatomist, J. B. Winslow, gave the name "sympathetic" to nerves which he demonstrated by dissection to lie outside the main cerebrospinal pathways. Neubauer (1772) published a superb illustration of the vagus and sympathetic nerves in the neck and thorax which ranks as one of the best anatomical plates that have been produced to date (Fig 3). Examination of this plate shows the high degree of perfection which had been reached by the gross anatomists at the end of the eighteenth century.*

As in other fields of medical science, anatomical knowledge developed far ahead of physiological experiment, but after Harvey's work on the circulation of the blood investigation of function by experiment began. Willis sectioned both vagus nerves in the dog and reported that there ensued "great trembling" of the heart. In 1669 Lower, one of his pupils, published the earliest observations on stimulation of the vagus. Further

* The nerve supply of the heart was also magnificently illustrated in the pen drawings of Antonio Scarpa in his *Tabulae neurologicae* (Pavia, 1795), with copper plates of Scarpa's drawings executed by Faustino Anderloni.

FIG. 1 Vesalius' illustration of the "sixth pair" of cranial nerves (according to Galen's classification).

The vagus nerve and the cervical portion of the sympathetic trunk are represented as one trunk. The thoracic and abdominal portions of the sympathetic chain and the rami communicantes are clearly shown. (From *De humani corporis fabrica*, ed. 2, Basel, 1555, p 512, reproduced through kind permission of Dr John F Fulton from the original now in Yale Medical Library Acknowledgment for legend is made to Sheehan, 1936, courtesy of *Archives of Neurology and Psychiatry*)

FIG. 2 Eustachius' conception of the cerebral origin of the cervical portion of the sympathetic trunk from the abducens nerve.

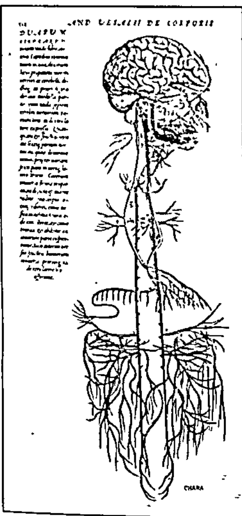
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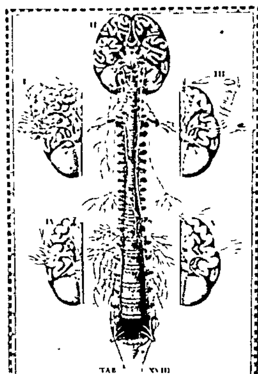


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The separate course in the neck of the vagus nerve and the sympathetic trunk had by this time been recognized. The superior cervical ganglion and some of the lower sympathetic ganglia are shown. (From *Tabulae anatomicae*, Amsterdam, 1722. Copperplates made in 1552 Reproduced through kind permission of Dr. John F. Fulton from the original now in Yale Medical Library. Acknowledgment for legend is made to Sheehan, 1936, courtesy of *Archives of Neurology and Psychiatry*.)

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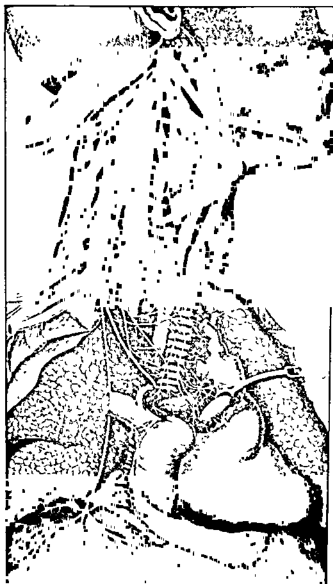


Fig. 3. Neubauer's plate of the cervical sympathetic and vagus nerves.

This superb engraving gives as accurate a picture of the innervation of the heart as any modern illustration prior to the discovery of the thoracic cardiac nerves in 1927 (compare with Fig 13) (From *Descriptio anatomica nervorum cardiacorum*, Frankfurt, 1772)

experiments by Ens (1745) and by the Webers (1846) a century later finally established the rôle of the vagus in inhibition of the heart. The discovery that the sympathetic trunks originate below the cranium and not from the brain stem, as described by Galen and all subsequent anatomists, was worked out by François-Pourfour du Petit in 1727. He was likewise the first to observe the pupillary paralysis which follows cervical sympathectomy, thus antedating Claude Bernard and Horner by over a hundred years.

The first appreciation of involuntary movements and visceral sensation developed out of the experiments of Whytt (1751). This man, who is little known in medical history, is really an outstanding figure. He was the first to gain an insight into such fundamental concepts as the tone of skeletal muscle, the reflex responses of the pupils to light, and the fact that "the distension of hollow muscle has a remarkable influence towards exciting them into action." Whytt's careful reasoning based on experiment first deflected the stream of medical thought away from the Galenic tradition of animal spirits and the theory that involuntary motion was dependent on the cerebellum. The ultimate expression of this theory had been reached in the writing of Willis, i.e., that "sympathy" was due to communications of the nerve tubes which issued from the cerebellum and brain stem, more especially those belonging to the "eighth pair" (the tenth in present terminology) and the "intercostal nerve." Whytt (1765) revised this traditional view by stating that "sympathy" presupposed feeling and must therefore be dependent on nerves. Moreover he drew the important deduction from his observations that nerve fibers were single units rather than anastomosing channels and that their activity was mediated through the brain and spinal cord. In the following quotation he not only gave the first suggestion of the neuron theory, but also of reflex action: "Since every individual nerve appears to be quite distinct from every other, not only in its rise from the medullary substance of the brain or spinal marrow, but also in its progress to that part where it terminates, it follows, that the various instances of sympathy, observed between the different parts of the body, cannot be owing to any communication or anastomosis of their nerves. . . . If, therefore, the various instances of sympathy cannot be accounted for from any union or anastomosis of the nerves, in their way from the brain to the several organs; and

if there are many remarkable instances of consent between parts whose nerves have no connection at all; it follows that all sympathy must be referred to the brain itself and spinal marrow, the source of all the nerves."

A more famous eighteenth century physiologist, but one whose deductions concerning the nervous system were less accurate, was Albrecht von Haller. In his treatise on sensation and irritability von Haller (1760) attributed sensibility to nerves, but postulated that irritability (contractility) was an independent function of muscle. He thereby delayed the development of the theory of reflex action already suggested by Whytt. Although von Haller discovered the sensibility of the parietal peritoneum, pleura, and pericardium to mechanical stimulation by experimentation, he believed that the apparent lack of sensation in the viscera was due to lack of nerve supply. Whytt, with his keener insight, had already suggested the idea of the "adequate stimulus." These two men were the first to make experimental studies on visceral sensibility.

In 1776 John Hunter, the great English anatomist, made the following observations: "If it is asked why the involuntary parts have nerves at all, the answer may be given that it is not for their common actions, but to keep up the connexion between the whole, for without them an animal would become two distinct machines, and one might be acting very contradictorily to the other; but by the intercourse between will and voluntary parts, between the voluntary and involuntary, and also between these last and the mind, an universal and uniform agreement or regulation is kept up, which communication produces one kind of sympathy." Hunter furthermore noted "that in joy or anger the heart beats quick or slow according to those states; sickness may be produced, purging, and contraction of the bladder." He also felt that in digestion the action of the stomach was controlled by the sympathetic nerves rather than by the cerebral masses.

In the first half of the nineteenth century work on the autonomic nervous system was pursued with increasing activity in France and Germany. The impetus for this was given by Xavier Bichat (1800, 1801, and 1802), a brilliant anatomist and physiologist who died in 1802 at the age of thirty-one. He pointed out that the nervous system regulated "la vie organique" and

"la vie animale," viz., its visceral and somatic functions in modern terminology, but he made the error of thinking that this integration took place in the ganglia and not through the spinal cord. Bichat anticipated Cannon's ideas of homeostasis by observing the effect of the "will" over animal life and the effect of emotion on the circulation, respiration, digestion, and the secretory glands. He also originated the ideas which have recently been stressed by Crile (1938), calling attention to the inferior evolution of the brain in many of the lower animals in comparison with the extensive development of the sympathetic plexuses. Bichat referred to the autonomic nervous system as the "système des ganglions" and not as the "vegetative nervous system." Credit for this term, commonly attributed to him, should be given to his pupil Reil (1807).

Although earlier workers had recognized that the viscera were not under voluntary control of the nervous system, they had not observed the structural difference between skeletal muscle and the muscular coats of the hollow viscera. This discovery was made by Johannes Müller (1840). Even he did not recognize that arteries possess a true muscular coat. The histological description of the muscular layer in the media was given by von Kölliker (1849) and its innervation by a periarterial sympathetic plexus by Henle (1868).

The great work of Claude Bernard began with his studies on the influence of the nervous system on the regulation of chemical activity in the tissues. It seemed probable to Bernard that chemical changes between the blood and tissues could affect local temperature, and he therefore began to investigate the action of the sympathetic nerves in the control of circulation. In March, 1852, he described the increase in temperature which develops in the side of the head following section of the cervical sympathetic trunk: "All the part of the head which becomes hot after section of the nerve becomes also the seat of more active circulation. The arteries especially seem fuller and appear to pulsate more forcibly; this is distinctly seen, in the rabbit, in the vessels of the ear."

The corollary phenomenon, that stimulation of the trunk produces vasoconstriction, was published in Philadelphia by Brown-Séquard the following August. The discovery of the vasodilator nerves arose from Ludwig's observations in the preceding

year that stimulation of the chorda tympani nerve increased the flow of blood through the submaxillary gland. The vasodilator effect of stimulating the posterior spinal roots was observed by Stricker in 1877.

Bernard, in his work on the nervous regulation of the blood vessels, was interested primarily in the effect on tissue metabolism. This developed into his classic conclusion that the animal body became independent of its surroundings only after developing a mechanism for maintaining constancy of what he designated "le milieu intérieur" (the internal environment). Under this category he included control of body fluids: blood, lymph, cerebrospinal fluid, etc. He first pointed out the remarkable constancy in the composition of the body fluids, and inferred that the adjustments which regulate this delicate balance were carried out by the nervous system (1878). In Bernard's own words: "The stability of the *milieu intérieur* is the primary condition for freedom and independence of existence; the mechanism which allows for this is that which ensures in the *milieu intérieur* the maintenance of all the conditions necessary to the life of the elements. . . . These are the same conditions as are necessary for life in simple organisms; but in the perfected animal, whose existence is independent, the nervous system is called upon to regulate the harmony which exists between all these conditions."

One other important contribution of Bernard was the overthrow of Bichat's theory of the complete independence of the ganglionic nervous system. According to Bichat visceral reflexes were mediated outside the spinal cord through the peripheral ganglia. Bernard controverted this and stated that these reflex arcs run through the spinal cord. In this connection he made the statement that "the existence of centripetal sensory fibers must be admitted in the sympathetic as well as in the cerebrospinal system."

The detailed anatomy of the autonomic nervous system was explored with the improvement of the microscope and the introduction of the microtome by His in 1870. Ehrenberg in 1833 gave the first accurate account of cell bodies in the sympathetic ganglia, and Valentin three years later described the typical internal structure of these cells, in addition to noting the difference between gray and white rami communicantes. Two years

later Remak found that the sympathetic ganglion cells give off the unmyelinated nerve fibers, but it was a number of years before his views were accepted. Remak (1854), as recorded by Sheehan, described the sympathetic rami as follows: "The lower branch ('ramus communicans sympathicus s. revehens') was *gray* and soft in texture and contained many fine myelinated and unmyelinated nerve fibers. The latter type arose from the cells in the sympathetic ganglia and were distributed peripherally along the spinal nerve. The upper branch ('ramus communicans spinalis s. advehens') was *white* and of firmer texture and contained myelinated fibers. It could be traced centrally into both the dorsal and the ventral spinal roots. Some of the fibers were thought to arise within the spinal cord and end in the sympathetic ganglion, occasionally passing through one ganglion as a white bundle to end in a ganglion lower or higher in the chain." Sheehan continues: "Although the difference in color and texture between the gray and the white rami had been recognized for many years, Remak's account is one of the earliest clear descriptions. In spite of an observation by Beck (1846) that the cervical and sacral nerves possess only gray rami, there was still no thought of limitation of the white rami to the thoracic and the upper portions of the lumbar region. The rami communicantes were believed to have connections with both the dorsal and the ventral roots and possessed, therefore, both sensory and motor functions. The muscles innervated were nonstriated and gave rise to 'involuntary' motion."

From the preceding paragraphs it is evident that a great deal was known about the basic structure of the vegetative nervous system by the middle of the nineteenth century. While a hint of its two component divisions had been reached in Claude Bernard's (1858 *A* and *B*) classical experiments on the changes in blood flow through the submaxillary gland following stimulation of the sympathetic and chorda tympani nerves, no clear appreciation had been reached of the function of the vagus nerves Its cardio-inhibitor effect had been demonstrated by the Webers in 1846, but it was still not considered as a part of the ganglionic nervous system. Further confusion existed as to the rôle of the intracranial ganglia, viz., the ciliary ganglion, which had been described by Willis in 1683; the sphenopalatine and submaxillary ganglia, described by Meckel (1749) and discovered separately

by Arnold (1827) and Brachet (1842); and the otic ganglion. In addition to these structures within the skull, the submucous and myenteric plexuses of the intestine had been described by Meissner in 1857 and by Auerbach in 1864.

The final discovery of the antagonistic action of the two component divisions of the autonomic system was made by Gaskell and Langley. The work of these brilliant English investigators left few extensive gaps in the anatomical and physiological understanding of the autonomic system and opened the field of treatment of visceral disease to the surgeon.

Gaskell (1886) studied the formation of the peripheral autonomic plexuses and described the three divisions of finely myelinated neurons which are given off from the neural axis in its cranial, thoracolumbar, and sacral levels. From a study of these structures he observed that "each nerve fibre leaves the central nervous system as a fine medullated nerve fibre which passes directly into its appropriate ganglion, and there in consequence of communication with one or more of the ganglion cells loses its medulla and passes out not as a single non-medullated fibre but as a group of non-medullated fibres. Such ganglion cells . . . assist in the conversion of a single nerve fibre into a group of fibres."

As a result of these observations Gaskell (1916) formulated the term "involuntary nervous system" and defined it as a "system of motor nerve cells to involuntary structures." Sheehan (1936) has credited Gaskell with being the first to recognize the existence of two antagonistic systems of nerves for the control of involuntary musculature and glandular secretion, one excitatory and the other inhibitory. In 1886 Gaskell wrote: "The evidence is becoming daily stronger that every tissue is innervated by two sets of nerve fibres of opposite characters so that I look forward hopefully to the time when the whole nervous system shall be mapped out into two great districts of which the function of one is katabolic, of the other anabolic." In view of Langley's work which followed, this was a prophetic statement.

Langley's final establishment of the two great divisions of the involuntary nerves depended on Hirschmann's discovery in 1863 that moderate doses of nicotine prevent pupillary dilatation when the cervical sympathetic trunk is stimulated. In experi-

ments with Dickinson in 1889 Langley found that nicotine acts by paralyzing the synapses between the preganglionic and postganglionic neurons in the sympathetic ganglia, and that in the case of the nerves which dilate the pupil and constrict the vessels to the ear these junctions are situated in the superior cervical ganglion. Following out this line of investigation Langley was able to map out the position of the cell stations and distribution of most of the "preganglionic" and "postganglionic" neurons, which he so named in 1893. In 1898 he proposed the name "autonomic nervous system" to include the cranial, thoracolumbar, and sacral pathways. Since he was unable to prove that the cells of the Meissner and Auerbach plexuses were a part of the bulbar and sacral pathways, he referred to them in a separate category as the "enteric nervous system."

The functional distinction between the thoracolumbar and craniosacral divisions of the autonomic system followed the discovery of epinephrine, which was made by Oliver and Schäfer in 1895. The similarity between the action of epinephrine and stimulation of the thoracolumbar fibers, and also the phenomenon of the exaggerated response to the drug after ganglionectomy, were described by Langley in 1901 and also by Elliott (1905). This functionally and anatomically distinct portion of the autonomic outflow was designated the "sympathetic." Subsequently Langley (1905) found that pilocarpine and other drugs act in a similar way on structures innervated by the finely myelinated fibers which originate from the cranial and sacral portions of the neural axis, and named this the "parasympathetic" division.

It should be observed at this point that although Langley primarily investigated the motor innervation of the viscera, he also (1903) observed large medullated axons in the peripheral autonomic plexuses which he described as sensory fibers because of their resemblance to ordinary sensory fibers in cutaneous nerves.* He believed that they passed through the ganglia without interruption and that they arose from the posterior sensory root ganglia.

* These large medullated axis cylinders had been observed by Gaskell (1886) and illustrated in Plate II, Figs 8 and 9. Edgeworth (1892) later studied these fibers at Gaskell's suggestion and concluded that they carried visceral sensation.

More recent work of great pharmacological and clinical importance has been done following Loewi's fundamental discovery in 1921 that the parasympathetic nerve impulse is actually propagated to smooth muscle cells by a chemical mediator which resembles acetylcholine. In the same year Cannon and Uridil reported chemical mediation of the nerve impulse in the sympathetic division by a substance secreted at the nerve endings which is closely related to epinephrine, viz., sympathin. Space does not permit an account of the methods which led to present knowledge of chemical mediation, but much of this which has a bearing on surgical problems is reviewed in Chapter V.

In recent years Cannon has completed the work begun by Claude Bernard, developing the rôle of the autonomic system in adapting the organism to shifting environmental and psychic changes. Readers who are interested in this field should refer to his monograph, *The Wisdom of the Body*, which gives a summary of his investigations and an excellent exposition of his deductions on the maintenance of "homeostasis."

The brilliant work of Gaskell and Langley on the peripheral autonomic plexuses has been carried upward into the brain, where investigation of the effects of stimulation of the hypothalamus begun by Karplus and Kreidl in 1909 and of destruction of nuclear masses by Ranson and his colleagues (1939) has located the central autonomic ganglia in the diencephalon. An insight into the superimposed function of the cerebral cortex and its inhibitory effect on the lower centers has been obtained from Goltz's (1892) early experiments on the decorticate dog. He was the first to observe that after removal of the cortex animals develop manifestations of rage with evidence of intense activity of the sympathetic nervous system. Nothing further need be said in this historical outline concerning the development of anatomy, physiology, and other aspects of laboratory investigation. The present conception of these fundamental subjects is described in Part I, and their clinical importance, which is so closely interwoven with the neurosurgical treatment of cardiovascular and visceral disease, is further discussed in Part II.

To complete the historical background it is only necessary to discuss the beginning of surgical intervention. Alexander (1889) of Liverpool appears to have been the first surgeon to operate

on the sympathetic nervous system. He performed cervical sympathectomy for epilepsy. The Roumanian surgeon Jonnesco (1896) later tried this operation on a large series of epileptics. Jaboulay (1899) of Lyons resected the lower cervical sympathetic chain for exophthalmic goiter. None of these procedures was strikingly successful, and as a result surgical interest in the sympathetic nervous system temporarily died away.

The first successful clinical application of sympathectomy was based on the work of François-Franck (1899). In this he stated that: "The entire sympathetic system is endowed with direct sensory fibers and carries centripetal fibers from the heart and aorta to the cord and the brain stem. It seems logical to assume that sympathectomy acts as much in suppressing abnormal afferent impulses to the higher centers as in blocking efferent stimuli to the thyroid and heart. This new idea of aortic pain carried by the cervicothoracic sympathetic nerves suggests the thought of trying their resection in angina pectoris." An interval of many years elapsed before Jonnesco (1920) began to put these ideas to a test. His first case in 1916 was brilliantly successful and was the beginning of modern operations on the cardiac nerves for the relief of angina pectoris. Particular credit is due to Professor René Leriche of the Collège de France for his continued emphasis on the efficacy of sympathectomy in the relief of various forms of visceral and vascular pain.

In 1913 Leriche called attention to the effect of periarterial sympathectomy in increasing the flow of blood to the extremities. Hunter (1924) and Royle (1924) later advocated sectioning the sympathetic rami for the reduction of excessive muscle tone in spastic paralysis. Although this treatment has not been generally accepted, its by-products have proved to be of extraordinary value. After these operations they noted that coincident vasomotor paralysis caused a striking increase in the circulation to the extremities. This observation led to the present surgical treatment of Raynaud's disease and other types of vasomotor spasm by sympathetic ganglionectomy. Leriche's publications and the visit of Hunter and Royle to this country in 1924 have been largely responsible for the stimulation of American investigation in the surgical problems of the sympathetic nervous system.

The reader who is interested in gaining further information

about the growth of the present-day understanding of the autonomic nervous system should consult the historical paper published by Sheehan (1936). This contains a wealth of interesting data and an extensive bibliography. The author and the editors of the *Archives of Neurology and Psychiatry* have very kindly permitted us to quote numerous passages and to reproduce two of the figures. This article has been of inestimable value to us in preparing this chapter and we wish to express to Professor Sheehan our appreciation and gratitude.

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Chapter III

ANATOMY OF THE AUTONOMIC NERVOUS SYSTEM

In a monograph devoted to the surgical aspects of the autonomic nervous system space prevents discussing the finer anatomical and embryological details. In this chapter, therefore, it has seemed best to take up the fundamental arrangement of the system as a whole, and to discuss its terminal ramifications mainly from the viewpoint of their possible interest to the surgeon. More will be said concerning regional anatomy in later chapters on surgical technic and the innervation of individual organs such as the heart. The best gross anatomical description of the peripheral autonomic plexuses is to be found in the monograph of Hovelacque (1927). For a detailed neuro-histological study the reader is referred to Ranson's textbook (1939) or to Kuntz's extensive monograph on the autonomic nervous system (1934), and also to the German texts of Müller (1931) and Stöhr's *Microscopic Anatomy of the Vegetative Nervous System* (1928).

I. Terminology

At the very beginning of this chapter it is important to define the general terminology which will be used. Gaskell and Langley classified the autonomic nervous system into two main anatomical and functional divisions: the sympathetic or thoracolumbar outflow, which leaves the spinal cord over its anterior roots between the first thoracic and second lumbar segments; and the parasympathetic or craniosacral division. The vagus carries the major portion of the cranial parasympathetic axons, but similar fibers also run in the oculomotor, facial, and glossopharyngeal nerves. The sacral parasympathetic outflow leaves the spinal cord with the second, third, and fourth sacral nerves

in the cauda equina. Physiologically and pharmacologically, as well as anatomically, the sympathetic and parasympathetic systems are very different. These differences were pointed out by both Gaskell (1916) and Langley (1921), and have been more completely developed in the work of Cannon (1929). It is necessary to bring out the essential points of this classification here, although the anatomical and physiological differences must be discussed and amplified in the separate chapters which follow. For the purpose of greater clarity this may be set down in the following form:

THE { AUTONOMIC or INVOLUNTARY or VEGETATIVE } NERVOUS SYSTEM

CRANIOSACRAL or PARASYMPATHETIC DIVISION	THORACOLUMBAR or SYMPATHETIC DIVISION
From: Cranial Nerves III, VII, IX, and X Sacral Nerves 2, 3, and 4	From: Thoracic Nerves 1–12 Lumbar Nerves 1 and 2

II. Embryological Development

It is not within the scope of this surgical monograph to delve deeply into the embryology of the autonomic nervous system. This aspect is taken up with great thoroughness in Kuntz's textbook (1934). A simple exposition, however, is necessary for a basic understanding of the functions of these nerves.

In studying the growth of the nervous system in the human fetus, embryologists have shown the close relationship between the sympathetic and the spinal nerves. The primordial anlage of the former appear early in embryonic development and are composed of cells which migrate peripherally from the neural tube. Froriep (1908) traced these cells from the primitive neural tube into the sympathetic trunks via the ventral nerve roots (Fig. 4). Kuntz (1934) has succeeded in tracing cells from these trunks into primordia of the celiac and other prevertebral plexuses of the abdominal viscera in the six millimeter human embryo. The development of the adrenal medulla also takes place by a migration of cells from the neural canal (Fig. 5). Chromaffin tissue thus represents a special differentiation of the terminal sympathetic neuron cell (*cf.* p. 109).

The vagus nerves likewise develop by cells migrating out from the hindbrain. Cells identical with those in the ganglionic cell clusters are present in abundance in the distal parts of the growing vagi. According to Kuntz (1909) the vagus forms the cardiac, pulmonary, and esophageal plexuses, whose primordia are already visible in the eight millimeter embryo, whereas cells migrating out from the thoracolumbar segments

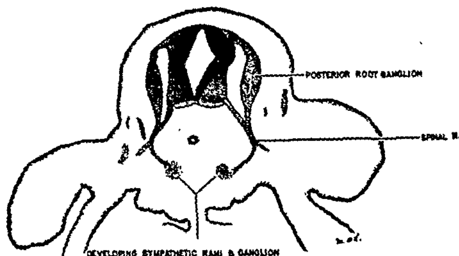


Fig. 4 Embryological development of sympathetic ganglia. Transverse section through the thoracic region of a 7 mm. human embryo. (Modified from Kuntz, 1934, courtesy of Lea and Febiger)

of the spinal cord lay down the gastrointestinal and pelvic plexuses. At a later stage of embryonic development outgrowing neurons of the opposite system invade each of these peripheral plexuses and thereby complete the characteristic dual innervation. Considerably less is known about the development of the autonomic ganglia in the head. Carpenter (1906) described the primordium of the ciliary ganglion in the chick as made up of cells which are displaced from the midbrain via the oculomotor nerve. It is assumed that the sphenopalatine, ciliary, and submaxillary ganglia arise from cells derived from the Gasserian ganglion.

The autonomic system, therefore, in both its cranial and thoracolumbar divisions, is developed from migrating cells which leave the brain stem and spinal cord in the early stages of embryonic development. These cells continue to divide by mitosis

and thus form the peripheral visceral plexuses. Consequently, there is no fundamental difference between the autonomic and the cerebrospinal neurons.

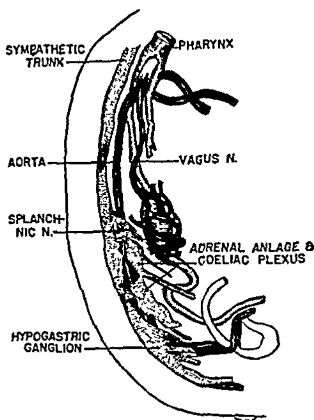


FIG. 5. Development of the adrenal glands and celiac plexuses. 10.5 mm. human embryo. (Redrawn from Brüning and Stahl, *Die Chirurgie des vegetativen Nervensystems*, Julius Springer, Berlin, 1924, with permission.)

III. Anatomy of the Cranial Autonomic Centers

Cortical Representation of the Autonomic Nervous System. Evidence will be presented in the following chapter that there is a cortical representation of the autonomic system. The cells from which these highest motor neurons arise have been found by Hoff and Green (1937) and Green and Hoff (1937) to lie in the premotor cortex, as well as at scattered points in the motor area, and in the marginal and cingulate gyri anterior to the central sulcus in monkeys.

The Autonomic Centers in the Diencephalon (Hypothalamus). *Localization of autonomic control* becomes more apparent in the diencephalon, and increasingly distinct in the

medulla and spinal cord. The cerebellum, on the other hand, plays only a minor part in autonomic regulation (see p. 70). Outstanding anatomical studies on the nuclei in the human hypothalamus which have been shown to coördinate visceral activity and, to a large extent, to integrate the autonomic responses commonly associated with emotional expression, have been carried out by Clark (1938) and others. This work has been recently summarized by Rioch, Wislocki, and O'Leary (1940). Phylogenetically there has been little change in this ancient group of nuclear masses and a certain fundamental ground plan is constant throughout the mammalian series (Grünthal [1933]). Clark lists sixteen nuclear areas in the human hypothalamus. The most important of these are the (1) preoptic, (2) supraoptic, (3) paraventricular, (4) posterior hypothalamic, (5) ventromedial hypothalamic, (6) dorsomedial hypothalamic, and (7) mammillary hypothalamic. The position of these is shown in Figure 6A.

The fundamental significance of all these structures is by no means clear, but there is evidence to support Beattie's (1935) suggestion that the preoptic nuclei are concerned with parasympathetic functions, the paraventricular and more caudal group with the sympathetic, and the more laterally situated nuclear areas with both. (For a more detailed discussion, see p. 70.) In addition the supraoptic nucleus gives rise to the supraopticohypophyseal tract and thereby regulates the secretion of the posterior lobe of the pituitary body. The action of the mammillary nuclei is uncertain It has been suggested that they bring the olfactory areas into relation with the taste centers in the hypothalamus, and these in turn with the cerebral cortex through the medium of the anterior thalamic nuclei. Connections between the hypothalamus and the olfactory areas, the corpus striatum, and the thalamus (somatic sensory) probably account for visceral symptoms associated with bad tastes, smells, and painful sensations.

Autonomic Centers in the Midbrain and Medulla. Anatomical studies show that autonomic regulation is transmitted to the peripheral plexuses through a series of nuclei in the midbrain, pons, and medulla. These lie close to the midline beneath the sylvian aqueduct and the floor of the fourth ventricle (Fig. 6B). The pupillary constrictor center is an integral part of the oculo-

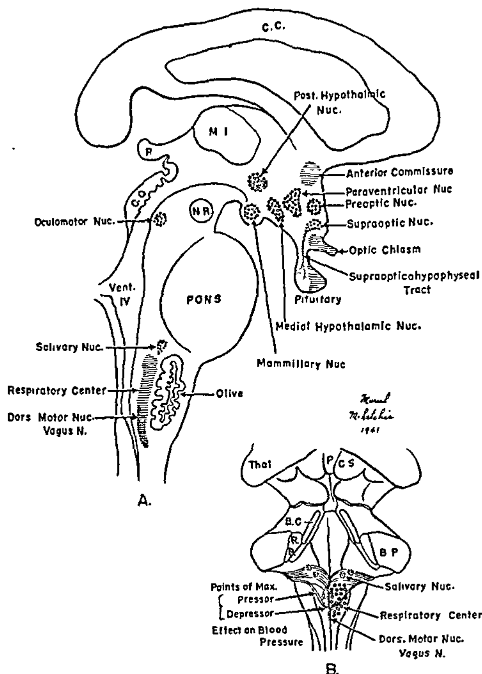


FIG 6. Important nuclear areas and centers for autonomic activity in the brain stem

A. Midline sagittal section. B. Dorsal view of medulla oblongata.

B C. Brachium conjunctivum.
B.P. Brachium pontis
C C Corpus callosum
C Q Corpora quadrigemina
C.S. Colliculus superior
M.I. Massa intermedia.
Thal Thalamus.
N R Nucleus rubor.
P Pineal.
R.B Restiform body.

(These figures are based on the work of Ranson and Billingsley, 1916; Clark, 1938; Ranson, 1939; and Pitts, Magoun, and Ranson, 1939.)

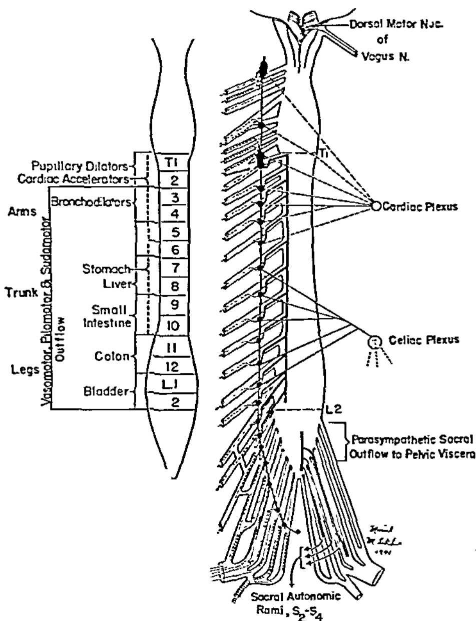
motor nucleus in the upper mesencephalon. At the junction of the pons and medulla the salivary nucleus is located in the reticular formation between the facial nucleus and the nucleus ambiguus (Ranson, 1939). The dorsal motor nucleus of the vagus lies at the level of the latter structure, just beneath the floor of the fourth ventricle. Two particularly important reflex centers are situated in the medulla oblongata. These consist of the respiratory and vasomotor centers. Both areas have been located with considerable accuracy. The former lies in the ventral reticular formation immediately over the inferior olive (Pitts, Magoun, and Ranson, 1939). The vasomotor center lies in the medulla as a strip along the floor of the fourth ventricle and runs from the facial colliculus to terminate a short distance rostral to the calamus scriptorius (Ranson and Billingsley, 1916*A*). It is closely associated with the dorsal motor nucleus of the vagus.

Autonomic Pathways in the Brain Stem and Spinal Cord. Anatomical knowledge of the descending pathways for impulses from the hypothalamic centers to the nuclei in the middle and hind brain, and to the spinal centers is still far from complete. Degeneration studies following posterior hypothalamic lesions led Beattie, Brow, and Long (1930) to conclude that fibers descending in the periventricular gray matter and in the medial longitudinal fasciculus of Schütz constituted the efferent hypothalamic pathway. These fibers become more medially placed at lower levels and were traced directly to the spinal cord. Magoun (1940) has described more recent investigations which have been carried out in Ranson's laboratory with the technical advantage of direct stimulation of the hypothalamic areas and observations on the effect of circumscribed lesions in the brain stem and spinal cord. These experimental studies "confirm the presence of some periventricular and medially situated connections descending from the hypothalamus, but indicate that of far greater importance is a pathway which runs backward from the lateral hypothalamic area through the tegmentum of the midbrain and pons, to traverse the lateral part of the reticular formation of the medulla, and descend in the ventro-lateral column of the spinal cord. . . . This pathway is made up of both ipsilateral and crossed connections, with crossing occurring both in the brain stem and at spinal levels."

Evidence confirming the existence of a similar pathway in man has been obtained by List and Peet (1939) from observation of alterations in sweat secretion in a series of lesions of the brain stem and by Foerster (1936), who has made a study of autonomic disturbances after anterolateral cordotomy and other lesions in the upper cervical segments.

Studies made on human beings after unilateral injuries to the spinal cord and animal experiments made by stimulating the hypothalamic centers after similar experimentally produced lesions have given an insight into the descending autonomic pathways in the spinal cord. According to Harrison, Wang, and Berry (1939) hypothalamic impulses may descend in the spinal cord uncrossed, or cross in the brain stem or in the spinal cord below the cervical segments. It is also known that some functions are bilaterally represented (vasomotor), some entirely unilateral (pupillary dilators). In the thoracic cord these descending sympathetic axons finally establish synapses with sympathetic motor cells in the intermediolateral column. This column lies in the lateral horn of spinal gray matter and gives off the sympathetic axons to the peripheral ganglia (Fig. 7).

The visceral afferent fibers enter the spinal cord in the posterior roots. There has been much disagreement concerning the transmission of visceral pain from this point on, but recent evidence (summarized in Chapter VI) indicates that these impulses are transmitted to the thalamus over higher sensory neurons which are similar to those that carry pain from other portions of the body. Their cells lie in the posterior horn of gray matter and their axons cross in the anterior commissure to ascend in the spinothalamic tract on the opposite side. Anterolateral cordotomy, provided the section is carried down to the gray matter, abolishes most forms of visceral pain in man, but Davis, Hart, and Crain (1929) have found that in animals this operation does not entirely abolish painful reactions when the gall bladder is distended. From observations made during colonmetrograms and cystometrograms after bilateral transections of the spinothalamic tracts, we have found that human beings also retain a sensation of discomfort as the walls of the hollow viscera are stretched. Dr. R. S. Morison, associate in anatomy at the Harvard Medical School, has suggested to us the possibility that these sensations may run for considerable distances over the



ateral cell column and its segmental outflow of preganglionic axons.

——— Preganglionic axon. – – – Postganglionic axon.

tracts of Lissauer. These tracts, which are composed of unmyelinated and finely myelinated fibers, run with, but are anatomically quite distinct from, the posterior columns. Ranson and Billingsley (1916*B*) have suggested that they are an alternate pathway for pain and that there are connections between them and the spinothalamic tracts.

IV. The Thoracolumbar Division

The Paravertebral Sympathetic Ganglia and Their Rami Communicantes. The paravertebral ganglionated chains run on either side of the vertebral column from the base of the skull to the ganglion impar at the coccyx (Fig. 8). The constituent ganglia are good-sized fibrous bodies and, together with their rami communicantes which connect them with the spinal nerves, constitute the only sympathetic structures which are seen by the casual student of anatomy. Throughout their length the chains are closely applied to the vertebral bodies, lying ventral to the transverse processes in the cervical spine, over the heads of the ribs in the thorax, and on the anterolateral surfaces of the lumbar vertebrae. There are commonly twenty-four ganglia in each chain, one corresponding to each spinal nerve except for the fifth lumbar and for five of the cervical segments. The chains fuse in front of the coccyx in the ganglion impar.

In the neck a condensation has occurred, there being only three or four ganglia for the eight cervical nerves (Fig 9). While the average ganglion in the sympathetic trunk measures about 3 to 5 mm. in length, the superior cervical and stellate ganglia are much larger. The former is a long fusiform structure, running beneath the carotid sheath from the base of the skull 2 to 3 cm. down into the neck. It is formed by a fusion of the ganglia connected with the three highest cervical nerves and sends gray rami to each of these.

Below the superior cervical ganglion the sympathetic trunk dwindles into a fine strand which runs on the deep fascia of the neck on the anterior surface of the longus capitis and longus colli muscles. In distinguishing the trunk from other nerves, the vagus runs within the fascia of the carotid sheath; when the vascular sheath is elevated on a retractor, the sympathetic trunk generally adheres to the underlying fascia. Furthermore, the

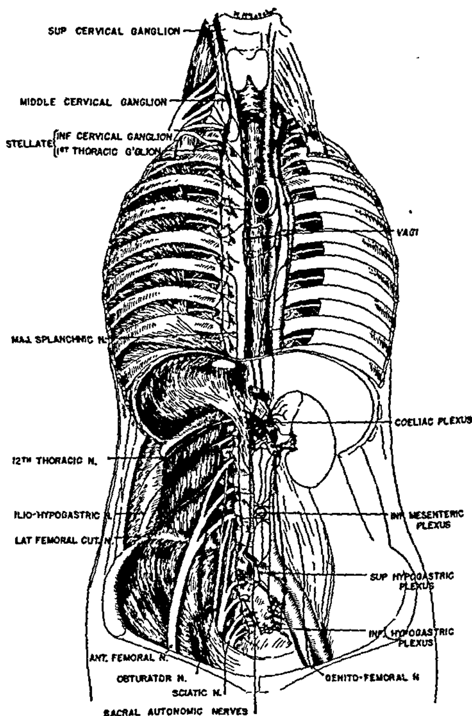


FIG. 8 The sympathetic gangliоnated chains and prevertebral plexuses.

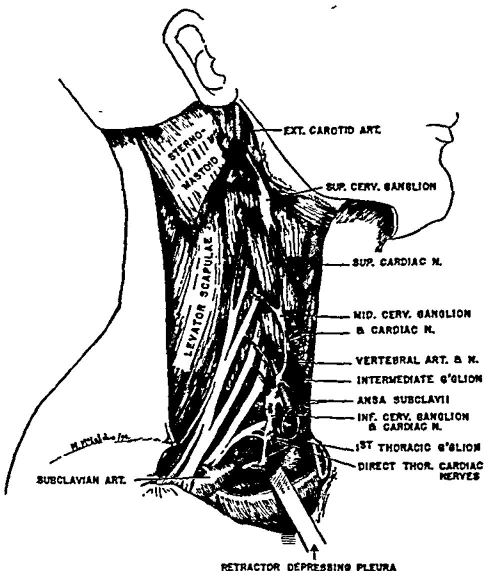


FIG. 9. The cervical sympathetic nerves.

trunk lies distinctly medial to the phrenic nerve, which originates from the third and fourth cervical nerves in this same plane. No other anatomical structure is likely to be confused with it.

The middle cervical ganglion, when present, lies at the level of the sixth cervical vertebra behind the inferior thyroid artery. It is formed by a coalescence of the fourth and fifth cervical ganglia. There is also a second and more constant ganglion situated in the lower cervical chain immediately anterior to the origin of the vertebral artery. This has been called the inter-

mediate ganglion by Jonnesco, Hovelacque, and Leriche. It is connected with the inferior cervical ganglion by two short fibers which encircle the vertebral artery, the ansa subclavii or annulus of Vieussens.

The inferior cervical and first thoracic ganglia are usually fused into a single dumb-bell-shaped structure known as the cervicothoracic or stellate ganglion. These paired ganglia may be completely fused, or they may appear as two quite separate structures. Usually there is a distinct isthmus between the two halves, the upper component giving off rami to the three lowest cervical nerves, while the lower is connected to the first thoracic nerve by a large and a smaller ramus communicans. This important structure lies between the head of the first rib and the vertebral artery at its junction with the subclavian. It often reaches a length of 2 cm. The remaining thoracic, lumbar, and sacral ganglia are much smaller and show frequent anatomical variations. These ganglia are distributing centers between the spinal cord and the unstriated muscle and glands of the entire body.

The central and peripheral connections of the sympathetic ganglia are shown in Figure 10. In the thoracic and upper lumbar segments of the cord each spinal nerve, on emerging from the intervertebral foramen, gives off a white ramus communicans to its corresponding sympathetic ganglion.* In addition to a small number of fibers of the somatic sensory type which will be discussed later, these white rami carry the so-called preganglionic axons. Their myelinated fibers originate in the intermediolateral cell column in the lateral horn of spinal gray matter, reach the spinal nerve over the anterior roots, and end in a sympathetic ganglion in synaptic relation (see below) with a number of postganglionic neuron cells. In contrast to the white rami, which connect the lateral horn cells in the cord with the sympathetic ganglia, the gray rami carry outgoing unmyelinated axons to the peripheral structures. The trophic cells of these fibers are situated in the sympathetic ganglia and their axons terminate in smooth muscle and glands throughout the body. In the case of the vasoconstrictor, sudomotor, and pilomotor fibers to

* It is worth pointing out that while the terms white and gray rami are appropriate from the angle of the neurohistologist in differentiating rami made up of axons that are largely myelinated or unmyelinated, the surgeon with either variety grasped in a nerve hook cannot distinguish between them.

the trunk and extremities, the postganglionic axons take origin in the paravertebral ganglionated chains and thence through the gray communicant rami rejoin the spinal nerve by which they are distributed to the periphery. In the case of the viscera the postganglionic neurons to the cardiac and pulmonary plexus also arise in the ganglia of the upper thoracic sympathetic chains. But the preganglionic fibers which make up the splanchnic, mesenteric, and hypogastric plexuses for the most part run through the paravertebral ganglia in continuity and end in the celiac, preaortic, and hypogastric ganglia. The postganglionic neurons which originate in these ganglia are therefore relatively short structures. This whole subject has been ably presented by Kuntz (1934).

It is important to remember that there are no white rami in the cervical, lower lumbar, or sacral segments. While some of the preganglionic axons end in the paravertebral ganglion to which a given white ramus leads and others run through it into the splanchnic plexuses (see Fig. 10), many others run either upward or downward over as many as three to six ganglia in the paravertebral chain (Langley, 1896). Eventually each terminates in a ganglion in synaptic connection with a number of postganglionic neuron cells. Ranson and Billingsley (1918) have counted the number of axons in the cervical sympathetic trunk and also the cells in the superior cervical ganglion and thereby computed that each preganglionic axon synapses with some twenty-two postganglionic fibers. *This is the reason for the diffuse nature of the sympathetic discharge.*

The important principle that the axons in the white rami do not run directly to the structures which they innervate, but form synaptic connections with a second set of neurons in the paravertebral or prevertebral ganglia, was discovered by Langley in 1900. Langley showed that these synapses could be blocked by painting the ganglia with nicotine, although stimulation of the gray rami still produced an undiminished response. His work showed that there are at least three orders of neurons in the sympathetic motor pathway: the first running from the central ganglia in the diencephalon to the lateral horn in the cord, a second group of preganglionic fibers from the lateral horn to the sympathetic ganglia, and a third of postganglionic fibers from the ganglia to the arteries, glands, and various viscera.

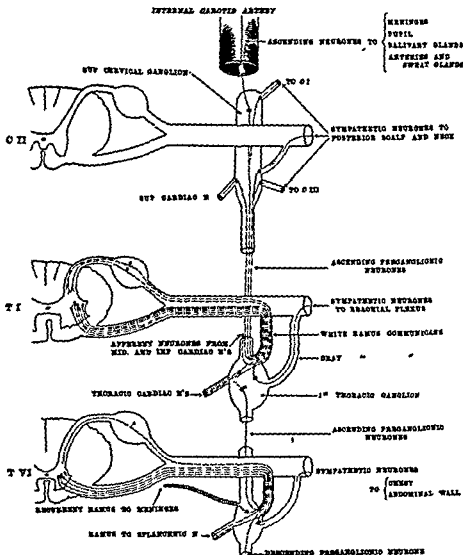


FIG. 10. Diagram of the peripheral visceral neurons.

— —·— Preganglionic motor neuron.
.... Postganglionic motor neuron.
— — — Viscerosensory neuron.

Langley's conception of a chain of neurons interrupted by synapses has recently been questioned by Stöhr (1938 and 1939). This well-known German microscopical anatomist has rejected the neuron doctrine as applied to the autonomic nervous system, and claimed that there is no interruption of the fiber pathway at the synapse. Sheehan (1941), however, has recently marshalled most convincing data against such a syncitial con-

ception. This includes evidence from comparative anatomy (Woollard and Harpman, 1939) and observations of fiber degeneration by Kuntz (1938 and 1940) and by Gibson (1940).

In contrast with the peripheral autonomic nerves, which are broken up into preganglionic and postganglionic neurons, visceral afferent neurons differ in no way from afferent neurons in the somatic system. Their cells lie in the dorsal root ganglia (Fig. 10). Like the fibers that carry somatic pain, they establish central connections in the spinal cord with cells in the posterior horn. Their long peripheral fibers traverse the posterior roots and the white and gray communicant rami. Instead of being interrupted in the sympathetic ganglia, as is the case with the motor fibers, their axons run directly to the peripheral plexuses in the visceral nerves.

Proof of the presence of sensory axons in the sympathetic trunks has been derived from a study of the histological characteristics of the constituent fibers (Edgeworth, 1892; Langley, 1903), as well as from their electrical conduction rates. From their work with the cathode ray oscillograph Gasser (1935) and also Heinbecker and Bishop (1935) concluded that different types of nerve fibers have varying rates of conduction. The most heavily myelinated variety, which are known to carry motor impulses to skeletal muscle, have the most rapid rate of conduction. These are not present in the autonomic nerve trunks. The less heavily myelinated as well as a few unmyelinated axons with progressively slower rates of conduction transmit sensory impulses, both somatic and visceral. A certain number of these are found in the vagus, as well as in the cardiac, splanchnic, and hypogastric plexuses, intermingled with a far greater number of visceromotor fibers. Of the latter the preganglionic axon is thinly myelinated, whereas the postganglionic is unmyelinated. From Ranson's (1939) description of the posterior roots it is known that the larger and more rapidly conducting afferent fibers enter the posterior columns, whereas other axons with little or no myelinization enter Lissauer's tracts. These are pain fibers. Both types are present in the visceral nerves, the former presumably transmitting visceral reflexes and remaining for the most part below the threshold of consciousness. Physiologically as well as anatomically, there is probably no fundamental difference betwen the viscerosensory fibers in the cardiac, splanch-

nic, and hypogastric plexuses and those which reach the skin through somatic nerves.

While all the ganglia in the paravertebral sympathetic trunks give off gray rami of nearly uniform size to the spinal nerves, the size of their visceral rami varies greatly. Some, such as the network given off by the cervical ganglia to the carotid artery, the thoracic cardiac, aortic, and ureteral nerves, are made up of such fine filaments that they can only be demonstrated by a special microdissection technic (Wharton, 1932). Others constitute very definite structures. The most important of the larger visceral branches are the superior, middle, and inferior cardiac and the splanchnic nerves. The former are given off from the corresponding cervical ganglia (Fig. 9). In the formation of the latter, the fifth * to the tenth thoracic segments contribute fibers to the major splanchnic nerve. The minor splanchnic originates from the tenth and eleventh, and is concerned largely with innervating the adrenal, while the twelfth thoracic segment gives off fibers to the least splanchnic nerve, which ends in the renal plexus (Fig. 11). Additional fibers are given off to the adrenal gland and kidney from the first and possibly from the second lumbar ganglia. A description of the distribution of their terminal plexuses is given on pages 50–52.

Since the craniosacral (parasympathetic) nerves also play a large part in the formation of the cardiac, pulmonary, splanchnic, and pelvic plexuses, the anatomy of the vagus and the sacral rami must be taken up prior to a discussion of the visceral plexuses.

V. The Craniosacral Division (Parasympathetic System)

The Vagus Nerve. The vagus is a mixed voluntary-involuntary nerve; its motor fibers to the pharynx and vocal cords, as well as its sensory fibers to the larynx, would appear to belong properly to the somatic system. Nevertheless, since the musculature in the pharynx and larynx have developed from the gill arches, the motor fibers, whose cell bodies lie in the nucleus ambiguus, have been classified as "*special* visceral efferent neurons" by American anatomists. This is in contradistinction to the "*general* visceral efferent neurons," which arise in the

* Additional higher rami, certainly from as high as the third thoracic ganglia, may enter the major splanchnic nerves.

Fig. 11. The splanchnic and vagus nerves.
For further details of renal and adrenal innervation see Fig. 58.

dorsal motor nucleus of the vagus and supply the heart, smooth muscle, and glands of the digestive tract. Below the larynx the greater portion of the vagal axons carry involuntary impulses and reflex afferent stimuli to and from the thoracic and upper abdominal viscera. The nerve originates in the medulla oblongata from three groups of cells (Fig. 12):

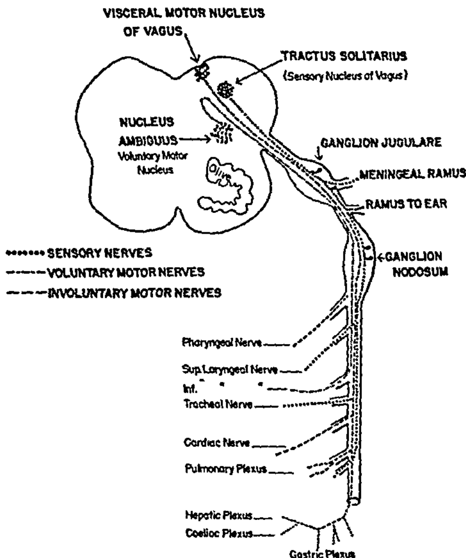


FIG. 12. Origins of vagus nerve.

(Modified from Bruning and Stahl, *Die Chirurgie des vegetativen Nervensystems*, Julius Springer, Berlin, 1924, with permission.)

a. The nucleus ambiguus—voluntary innervation of the striated muscle in the pharynx and vocal cords.

b. Dorsal motor nucleus—concerned with visceral motor innervation.

c. Fasciculus solitarius—sensory innervation of pharynx and larynx through neurons whose cells lie in the ganglion jugulare; visceral afferent innervation through neurons whose cells lie in the ganglion nodosum.

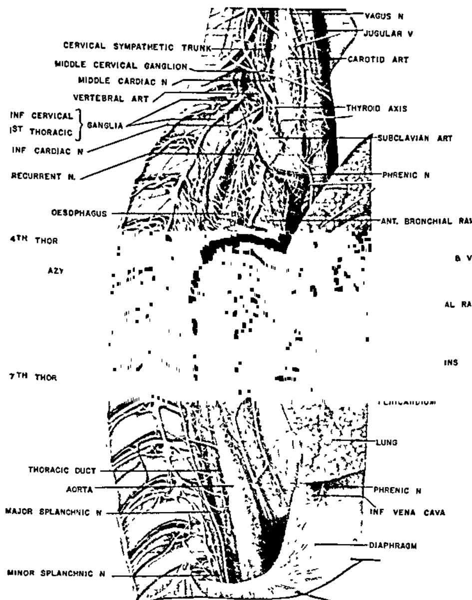


FIG. 13 Relations of the vagus and splanchnic nerves in the thorax (Reproduced from Braeucker, 1927)

The nerve leaves the skull through the jugular foramen, expanding at this point into the jugular ganglion and just below the foramen into the ganglion nodosum. These enlargements correspond to the dorsal root ganglia of the spinal nerves and contain the cells of the afferent neurons. At this level there are also many anastomoses with the glossopharyngeal and hypoglossal nerves, as well as numerous connections with the superior cervical sympathetic ganglion and the carotid sinus plexus. The course of the vagus in the carotid sheath and through the thorax is illustrated in Figure 13. In the thorax it establishes further connections with the sympathetic through the inferior cervical ganglion and then enters into the formation of the cardiac, pulmonary, and esophageal plexuses. Below the diaphragm the left vagus sends branches along the lesser curvature to the anterior wall of the stomach and a large ramus to the hepatic plexus (Fig. 11). The right vagus, which at this point lies behind the cardia, sends its fibers to the posterior wall of the stomach and through the celiac ganglion to the terminal plexuses in the upper abdominal viscera. Unlike the sympathetic, the preganglionic axons of the vagi run directly into the terminal plexuses in the walls of the viscera before forming synaptic connections with short, postganglionic fibers (Fig. 18). This arrangement results in a specific localized effect in contrast to the diffuse sympathetic discharge.

The Sacral Autonomic System. The sacral parasympathetic outflow leaves the spinal cord with the second to fourth sacral nerves in the cauda equina. After the mixed nerves have passed through the sacral sympathetic chains, the white rami are given off (Fig. 19). These pelvic nerves (nervi erigentes) do not pass through the sacral sympathetic chains, but run directly into the hypogastric ganglia and thence to the walls of the pelvic viscera. Their postganglionic neurons originate in the intrinsic plexuses of the genitalia, bladder, and rectum.

Other Parasympathetic Pathways. In addition to the vagus and sacral autonomic pathways, several lesser channels exist (Fig 14):

a. Pupillary-constrictor fibers.
b. Lachrymal fibers.
c. Fibers to the salivary glands.
d. Vasodilator fibers in the posterior spinal roots. This subject is discussed in Chapter IV, page 83. If such special fibers exist, there is no proof that they belong to the parasympathetic system.

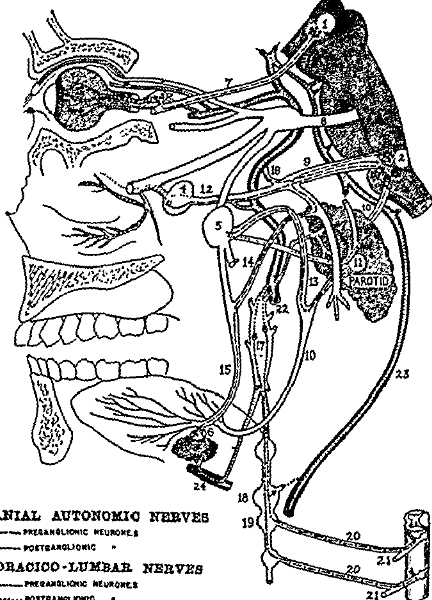


FIG. 14. The autonomic innervation of the head. (Modified from Hovelacque, 1927, courtesy of Gaston Doin et Cie., Paris)

1. Oculomotor nucleus.
2. *Superior and inferior salivary* nuclei.
3. Ciliary ganglion
4. Sphenopalatine ganglion.
5. Otic ganglion.
6. Submaxillary ganglion.
7. Oculomotor nerve
8. Trigeminal nerve
9. Facial nerve.
10. Glossopharyngeal nerve.
11. Auriculotemporal branch of trigeminal nerve.
12. Vidian nerve.
13. Tympanic branch of glossopharyngeal nerve.
14 Chorda tympani nerve.
15. Lingual nerve.
16. Branch of superficial petrosal nerve containing vasodilator fibers to carotid artery.
17 Superior cervical sympathetic ganglion
18. *Inferior cervical sympathetic* ganglion
19 First thoracic sympathetic ganglion.
20. White rami communicantes.

A final important anatomical principle is the mixed character of the autonomic nerves. The vagus carries sensory and motor fibers to the pharynx and larynx, as well as the cranial autonomic neurons. In the neck there are numerous anastomoses between it and the cervical sympathetic ganglia. In all the visceral plexuses a further mixing of the two systems takes place. This is important from a surgical angle, because it makes it difficult to paralyze one system exclusively and to leave the other entirely intact.

VI. The Peripheral Autonomic Plexuses

Having taken up the formation of the cranial and sacral portions of the parasympathetic, as well as the thoracolumbar sympathetic system, it remains to show how these two distinct sets of fibers are combined to form the individual peripheral plexuses. As many of these have yet to be attacked surgically and as those which are of importance to the surgeon will be discussed in subsequent chapters, the most satisfactory way of describing their general make-up is by the briefest possible skeleton outline. This section is intended to serve only as a reference, and not to be read through in continuity.

Autonomic Innervation of the Iris (Fig. 14)

a. Parasympathetic

In the first edition of this book it was stated that preganglionic neurons arise from cells in the Edinger-Westphal nucleus and run in the oculomotor nerve to the ciliary ganglion. Mitchell of Aberdeen has kindly called our attention to Clark's (1926) work on this subject in which he points out that the cells of this group give rise to no fibers which pass directly to the ciliary ganglion or the eye itself. Therefore the origin of the preganglionic fibers cannot be located more accurately than in the general area of the oculomotor nucleus.

Postganglionic neurons originate in the ciliary ganglion and run through the short ciliary nerves to the constrictor muscle of the iris.

Function: Contraction of pupil and accommodation.

Surgical application: None reported to date.

b. Sympathetic

Preganglionic neurons originate from cells in the intermediolateral column, enter the highest two thoracic white rami, and

21. First and second thoracic nerves.
22. Internal carotid artery.
23. Vertebral artery.
24. External maxillary artery.

ascend the cervical sympathetic chain to its superior cervical ganglion.

Postganglionic neurons originate from cells in the above ganglion, ascend in the carotid plexus to the ophthalmic division of the fifth nerve, then run via the nasociliary nerve to the eyeball.

Function: Dilatation of pupil, and widening of palpebral fissure.

Surgical application: Resection of the superior cervical sympathetic ganglion in cases of facial paralysis enables the patient to close his eyelids almost completely.

Innervation of the Lachrymal Glands

The pathway of impulses which stimulate the flow of tears has been described by Rowbotham (1939).

a. Parasympathetic

Preganglionic axons: Emerge from the brain stem in the facial nerve (nervus intermedius of Wrisberg), but branch off at the geniculate ganglion. From there they run in the great superficial petrosal and vidian nerves to the sphenopalatine ganglion.

Postganglionic neurons: Cells in Meckel's ganglion send fibers via the temporomalar branch of the second division of the trigeminal nerve to the lachrymal gland. According to Gray's *Anatomy* (1918) there are also filaments from the ophthalmic division.

Function: Stimulation of lachrymal cells and vasodilatation.

Surgical application: Abnormal lachrymal function after injury to facial nerve accounts for phenomenon of "crocodile tears" (see p. 262).

b. Sympathetic

Preganglionic neurons are the same as in the case of the eye.

Postganglionic neurons: Axons, which arise from cells in the superior cervical ganglion, ascend along the internal carotid artery. They branch off to the deep petrosal nerve and the vidian. From this point on their course is with the parasympathetic fibers

Function: Vasoconstriction.

Surgical application: None.

Innervation of the Salivary Glands (Fig. 14)

a. Parasympathetic

Preganglionic neurons to submaxillary and sublingual glands: Cells lie in nucleus salivatorius superior and send their neurons through the facial, chorda tympani, and lingual nerves directly to the submaxillary and lingual glands.

Postganglionic neurons: Cells lie along chorda tympani nerve.

Preganglionic neurons to parotid gland: The cranial autonomic

neurons to the parotid gland arise in the inferior salivary nucleus and leave the brain in the glossopharyngeal nerve. They then pass into the tympanic branch (nerve of Jacobson) to reach the otic ganglion via the lesser superficial petrosal nerve.

Postganglionic neurons: From the otic ganglion the terminal axons reach the parotid over the auriculotemporal branch of the trigeminal nerve.

The anatomy of the salivary pathways has been worked out in dogs. In man Reichert and Poth (1933) have observed that section of either the seventh or ninth cranial nerves causes a decrease in salivary secretion in both the submaxillary and parotid glands.

Function: Increases salivation and dilates blood vessels.

Surgical application: None reported to date.

b. Sympathetic

Preganglionic neurons are the same as in the case of the eye.

Postganglionic neurons: Cells in superior cervical sympathetic ganglion send their fibers along the external carotid and external maxillary arteries to the glands.

Function: Also increases salivation, but causes vasoconstriction.

Surgical application: None.

Vasomotor Supply of Meningeal and Cerebral Arteries

a. Parasympathetic

Vasodilator neurons leave the brain in the facial nerve—Cobb and Finesinger (1932). At the geniculate ganglion these fibers enter the greater superficial petrosal nerve, which Chorobski and Penfield (1932) have shown gives off a small group of fibers to the sympathetic plexus on the internal carotid artery.

Sensory neurons: Penfield and McNaughton (1940) have studied the sensory innervation of the dura by examination of cleared specimens and also by direct stimulation in patients under local anesthesia. They have found that the falx and tentorium receive fibers from the ophthalmic division of the trigeminal nerve and that the second and third divisions supply the middle meningeal artery and a considerable portion of the dura over the convexity of the skull. In the posterior fossa the vagus contributes a few sensory fibers to the region of the jugular bulbs and sigmoid sinuses.

Function: Meningeal and cerebral vasodilatation and transmission of afferent impulses.

Surgical application: Relief of certain forms of headache and atypical facial neuralgia.

b. Sympathetic (Fig. 14)

Preganglionic neurons: Cells lie in intermediolateral column and send their axons over the upper two thoracic white rami to the stellate and superior cervical sympathetic ganglia.

Postganglionic neurons: These are given off from both ganglia and enter the skull over two pathways:

1. From the stellate ganglion via the vertebral nerve a plexus ascends the vertebral and basilar arteries.
2. A second larger plexus originates from the superior cervical sympathetic ganglion; one division follows the external carotid and middle meningeal arteries to innervate the meninges, and another the internal carotid artery to the circle of Willis.

Sensory neurons: None.

Function: Meningeal and cerebral vasoconstriction and dilatation (Forbes and Wolff, 1928).

Surgical application: Of possible significance in migraine, because of vasodilator supply to branches of external carotid artery.

The Carotid Sinus Plexus (Fig. 15)

The bifurcation of the carotid artery derives a number of afferent fibers from the ganglion nodosum of the vagus and the glossopharyngeal nerves. These terminate in typical sensory end organs in the walls of the carotid bulb (de Castro, 1926–1928) and carotid body. The main carotid sinus nerve joins the glossopharyngeal and it has been demonstrated by Code and Dingle (1935) that section of this nerve in the dog removes the regulatory influence of the sinus on the heart rate and blood pressure. The sinus also receives efferent connections from the superior cervical ganglion of the sympathetic trunk. Hering (1927) and Heymans with his coworkers (1933) have shown that this small plexus has a highly specialized function as a reflex center for controlling blood pressure, heart rate, and respiration (*cf.* Chap. IV). An excellent description of this plexus with photographs of the structures has been published by Tchibukmacher (1938).

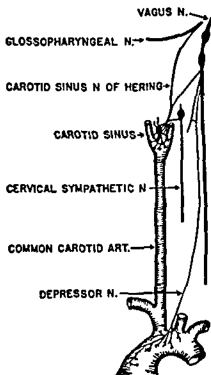


Fig. 15. The carotid sinus nerves

(Redrawn and slightly modified from Heymans, Bouckaert, and Regniers, 1933, courtesy of Gaston Doin et Cie., Paris.)

Surgical resection of the sinus has resulted in the cure of recurrent attacks of syncope and rare forms of convulsive seizures.

Cardiac Innervation (Figs. 13 and 16)

This anatomical scheme is based on the work of Nonidez (1939).

a. Parasympathetic

Preganglionic motor neurons originate in the dorsal nucleus of the vagus and end in the intrinsic cardiac ganglia.

Postganglionic fibers run from these ganglia along the coronary arteries.

Afferent axons from the intrinsic cardiac ganglia also reach the ganglion nodosum by way of the depressor portion of the vagus nerve. In certain animals and occasionally in man this constitutes a separate trunk, the nerve of Cyon and Ludwig (1866).

Function: Cardiac inhibition and probably constriction of the coronary arteries.

b. Sympathetic

Preganglionic motor neurons come from cells in the intermediolateral column via the anterior spinal roots and upper three to five pairs of white rami communicantes to enter the upper thoracic ganglia. Some of these form synapses at once; others ascend to the cervical ganglia.

Postganglionic neurons leave the ganglionated chain in two divisions: the upper via the superior, middle, and inferior cardiac nerves; the lower by the thoracic cardiac nerves, which have recently been described by Cannon, Lewis, and Britton (1926), Braeucker (1927), Jonnesco and Enarchesco (1927), Kuntz and Morehouse (1930), and White, Garrey, and Atkins (1933). Both sets of fibers converge in the anterior and posterior cardiac plexuses.

Sensory neurons, with cells in the upper thoracic posterior root ganglia (especially the second, according to Nonidez, 1939), run via the middle and inferior cardiac nerves, as well as in the thoracic cardiac nerves. These terminate in typical sensory end organs (Stöhr, 1928) in the adventitial plexuses of the aorta and coronary vessels, as well as in the pericardium and the walls of the heart. Heinbecker (1933) and Braeucker (1933) have also claimed that there are direct viscerosensory connections between the cervical ganglia and the posterior roots of the cervical nerves. Experience with cardioaortic pain referred to the neck makes us quite certain that such connections, if they exist, are of little clinical importance.

Function: Cardiac acceleration and the conduction of cardiac pain. The most widely accepted evidence indicates that these nerves also dilate the coronary arteries.

Surgical application: Relief of pain in coronary thrombosis, angina pectoris, aneurysm of the arch of the aorta, and in the control of paroxysmal tachycardia.

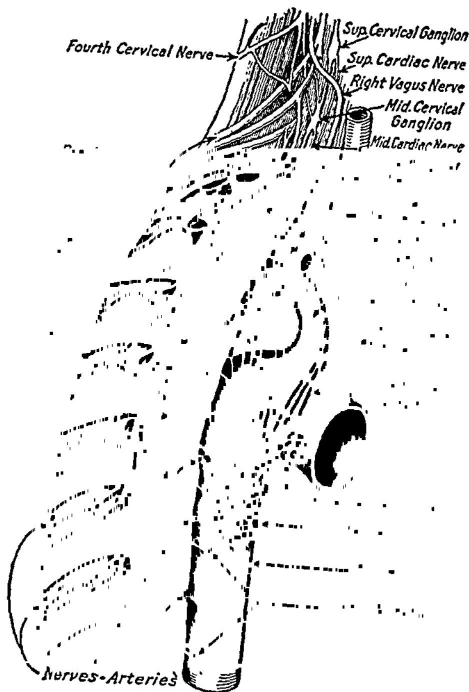


Fig. 16. The nerve supply of the heart.
(Modified from Kuntz and Morehouse. Reproduced from P. D. White, *Heart Disease*, Macmillan, 1931.)

Pulmonary Innervation

a. Parasympathetic

The most complete dissections of the nerve supply to the trachea, bronchi, and pulmonary vessels have been carried out by Braeucker (1927).

The preganglionic axons for the most part leave the vagi in the upper mediastinum. In Figure 13 three to four large and many smaller filaments can be seen leaving the vagus and running to the lung hilus. These form synapses with postganglionic neurons in the anterior and posterior pulmonary plexuses which are grouped around the main bronchi.

b. Sympathetic

The preganglionic sympathetic axons follow much the same course as the cardiac supply, except that fewer of them ascend into the cervical sympathetic trunks.

Postganglionic fibers run from the inferior cervical as well as the upper four thoracic ganglia to the pulmonary plexuses.

Function: The action of neither parasympathetic nor sympathetic divisions has been definitely worked out, beyond constriction and dilatation of bronchi (see p. 347).

Surgical application: There are numerous reports of operations on both the vagus and sympathetic trunks for bronchial asthma, but neither method has proved strikingly successful to date.

Esophageal Innervation

a. Parasympathetic (Fig. 13)

The thoracic esophagus receives its cranial autonomic innervation over a large number of small filaments directly from the vagus nerves.

Function: Stimulation of peristalsis.

b. Sympathetic

Sympathetic motor as well as viscerosensory fibers leave the cord mainly from its fifth and sixth thoracic segments. According to Knight (1934), dissections of stillborn infants show that the upper portion of the thoracic esophagus derives a few direct branches from the sympathetic ganglia at the level of the aortic arch. Immediately above the diaphragm no direct fibers run to the esophagus. This lower portion, as well as the cardiac sphincter, derives its innervation via the descending periaortic plexus and the splanchnic rami which run through the celiac ganglia and along the branches of the celiac axis (principally the left gastric artery)

Conduction of pain

Surgical application: Relief of pain in obstructive lesions of the esophagus; possibly for the cure of achalasia of the cardiac sphincter (cardiospasm), if recently reported work is corroborated.

Innervation of the Upper Abdominal Viscera (see also the anatomical description of the splanchnic innervation on p. 38)

Valuable descriptions of the nerve supply of the biliary system are available by Alexander (1940) and of the stomach by McCrea (1926).

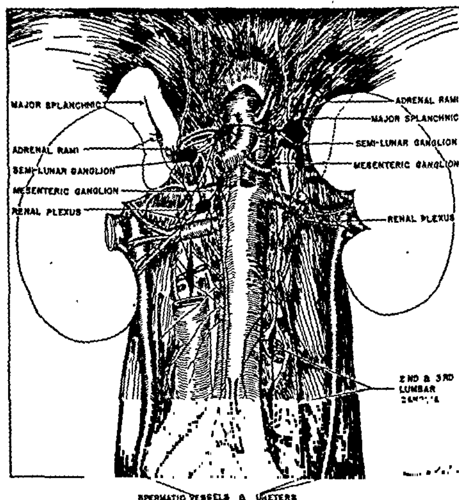


Fig. 17. The abdominal autonomic plexuses.

(*Modified from* Hovelacque, 1927, *courtesy of* Gaston Doin et Cie., *Paris*)

a. Parasympathetic

Preganglionic neuron cells lie in the dorsal vagal nucleus and send axons along the vagi to end in the intrinsic visceral plexuses. These are designated as the phrenic, adrenal, renal, spermatic or ovarian, gastric, hepatic, splenic, and superior mesenteric plexuses (Fig. 17). In the case of the intestine, it is probable that the fibers terminate around the ganglion cells of Auerbach's mesenteric and Meissner's submucous plexuses (Fig. 18).

Function: To stimulate peristalsis, secretion and vasodilatation of the digestive glands. While the vagi carry some afferent reflex stimuli and a part of the sensation of nausea, they are not known to carry any definite pain sensation.

Surgical application: Section of the lower vagi has been attempted to decrease acid secretion in peptic ulcer, but the results have been unimpressive.

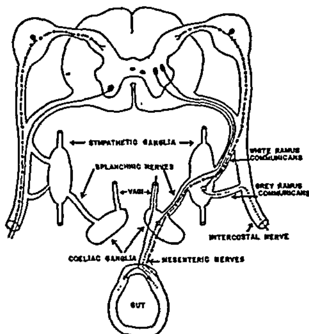


FIG. 18. Diagram of vagus and splanchnic nerve endings in intestine.

Left side: Somatic innervation
Motor neurons ———
Afferent neurons —·—·—

Right side: Visceral innervation.
Preganglionic neurons ———
Postganglionic neurons ....
Afferent neurons —·—·—

b. Sympathetic

Preganglionic cells lie in the intermediolateral column (Fig. 18). Their axons traverse the lower seven or eight pairs of thoracic white rami (Fig. 11), pass through the sympathetic trunk ganglia, for the most part without interruption, and along the splanchnic nerves to end in the preaortic ganglia. The celiac ganglia usually consist of two large semilunar masses on either side of the celiac axis with connections to lesser subsidiary ganglia grouped around the arteries to the other upper abdominal organs (Figs. 17 and 58).

Postganglionic fibers leave the celiac and other related ganglia to run with the vagal fibers along the periarterial visceral plexuses. In the peculiar case of the adrenal glands the preganglionic axons are not interrupted in extrinsic ganglia, but end around the chromaffin cells of the adrenal medulla. Presumably these post-

ganglionic cells have taken on a secretory function. In addition to the minor splanchnic nerves from the tenth and eleventh thoracic segments, further filaments to the adrenal glands are given off from the twelfth thoracic and first (and possibly second) lumbar segments.

Afferent pathways, with their cells in the lower six pairs of thoracic posterior root ganglia, follow a corresponding course along the sympathetic pathways to sensory endings in the mesenteries and walls of the hollow viscera (Fig. 18). Many of these fibers end in the Pacinian corpuscles (Sheehan, 1932).

Function: Inhibition of peristalsis, secretion, and vasoconstriction. The afferent fibers carry subconscious reflex stimuli, the feeling of nausea, and the pain of distention from the hollow viscera.

Surgical application: Relief of pain from the upper abdominal viscera in incurable disease.

Innervation of the Pelvic Viscera

a. Parasympathetic

Preganglionic neuron cells lie in the lateral portion of the anterior horn of the sacral cord. Thence their axons run out over the second, third, and fourth sacral anterior roots and the sacral nerves, to emerge from the sacral foramina in the hollow of the sacrum. Their rami, the nervi erigentes, pass through the inferior hypogastric ganglia. The distribution of these fibers was formerly supposed to be limited to the pelvic viscera. Mitchell (1935), however, has traced a number of ascending strands which carry parasympathetic axons via the inferior mesenteric plexus to the descending colon. Parasympathetic innervation of the uterus, tubes, ovaries, and testes has been demonstrated by Reynolds (1939), Mitchell (1938), Goecke (1938), and Wein (1939).

Postganglionic neurons constitute the intrinsic plexuses in the muscular walls and internal sphincters of the bladder and rectum, as well as in the genital organs.

Function: Contraction of the bladder and lower colon with relaxation of the involuntary sphincters. Vasodilatation.

There are also myelinated sensory axons in these nerves.

Surgical application: Section of the lower sacral posterior roots, chemical destruction of their fibers by intrathecal injection of alcohol, or resection of the inferior hypogastric plexus may be used as a last resort in painful malignant conditions of the pelvic viscera, but *these operations paralyze the voluntary power* of micturition and the anal sphincter.

b. Sympathetic pathways

Preganglionic cells lie in the lowest thoracic and upper lumbar levels of the intermediolateral column. These cells send their axons

out over the lower white rami of the thoracolumbar outflow to the lumbar and preaortic ganglia.

Postganglionic neurons originate in the sympathetic trunks, as well as in the preaortic ganglia, to form a plexus descending along

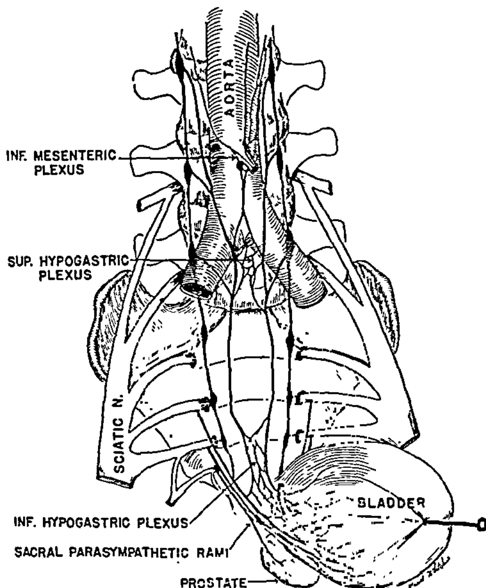


FIG. 19. The inferior mesenteric and hypogastric plexuses.

the abdominal aorta (Fig. 19). At the level of the inferior mesenteric artery there are two small ganglia, and from them a plexus descends this artery to innervate the sigmoid and rectum. The remainder of the descending sympathetic fibers form the superior hypogastric plexus at the bifurcation of the aorta. This divides into the two hypogastric nerves which run in the hollow

of the sacrum to join the inferior hypogastric plexus. An excellent surgical description of the superior hypogastric plexus has been given by Dobrzaniecki and Serafin (1934).

Sensory fibers from the posterior root ganglia in the same segments of the cord run directly into the superior and inferior hypogastric plexuses.

Function: Vasoconstriction and contraction of smooth muscle in the bladder neck, prostate, and seminal vesicles. Inhibition of peristalsis in the lower colon and constriction of the sphincter ani internus (the extent of this action is still uncertain). Transmission of certain forms of bladder and uterine pain.

Surgical application: Resection of the lumbar ganglia which give rise to these fibers, or the ganglia at the root of the inferior mesenteric artery and the superior hypogastric plexus, through which the sympathetic impulses pass, relieves the neurogenic form of megacolon. Excision of the superior hypogastric plexus alone relieves the pain of essential dysmenorrhea, but is less effective in painful conditions of the bladder.

Innervation of the Peripheral Arteries, Sweat Glands, and Erector Pilae Muscles

a. Parasympathetic

Investigations by Hinsey (1934), Westbrook and Tower (1940), and others (see p. 84) indicate that the vasodilator action of the posterior spinal roots does not depend on the presence of a parasympathetic outflow from the spinal cord, as suggested by Kuré (1931). In so far as is known, therefore, there is no parasympathetic supply to the peripheral blood vessels (flushing of the face from embarrassment may be an exception to this statement, but the nervous mechanism of this phenomenon has not been investigated). There are also no parasympathetic fibers to the erector pilae muscles, and no known connections with the sweat glands except in the skin around the mouth (List and Peet, 1938).

b. Sympathetic

Preganglionic neurons arise from the entire thoracolumbar portion of the intermediolateral column. Their axons emerge over the anterior roots and white communicant rami to terminate in all the ganglia of the paravertebral sympathetic chains.

Postganglionic neurons leave these ganglia in two ways:

1. Directly to the larger arteries of the trunk to form periarterial plexuses, e.g., along the aorta, carotid, subclavian (annulus of Vieussens), and iliac vessels. These plexuses do not descend far beyond the axilla and Poupart's ligament, but do ascend along the carotid and vertebral arteries to the head.

2. Gray rami run back into the cervical, intercostal, and the lower spinal nerves, and their axons are distributed in a segmental manner to the sweat glands, hair follicles, and all the arteries of the trunk and extremities (Figs. 20

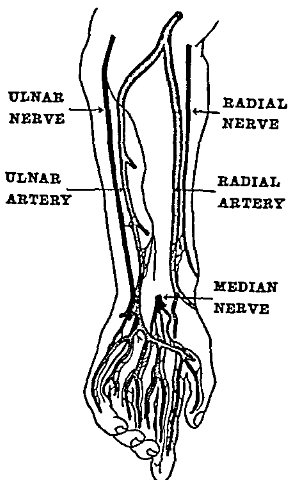


FIG. 20. The nerve supply of the arteries of the forearm and hand.

(Redrawn from Kramer and Todd, *Anatomical Record,* 1914, VIII, 243, with permission.)

and 21). Krogh (1929) has shown that the terminal ramifications of these unmyelinated axons run to the individual capillaries.

Sensory innervation of the arteries: Moore and Singleton's (1933) experiments have shown that painful stimuli from the visceral arteries are transmitted over sensory axons in the splanchnic and other sympathetic nerves, but that pain from the peripheral arteries traverses the spinal sensory nerves.

Surgical applications: Resection to increase blood flow in the extremities and for the relief of excessive sweating.

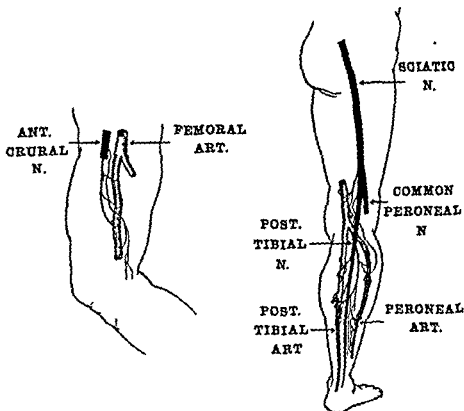


FIG. 21. The nerve supply of the arteries of the leg.
(Modified from Potts, *Anatomischer Anzeiger*, 1914, XLVII, 138. Courtesy of Gustav Fischer, Jena.)

This anatomical outline has been set down as briefly as possible because this ground will be covered again, both in the following chapter on physiology and from another angle in the discussion of surgical procedures on the sympathetic nerves. For further details there are a number of excellent books available, among which the following have been frequently quoted and deserve special mention: Hovelacque's *Textbook of Neuro-anatomy* (1927) for a complete discussion of gross anatomy and its excellent plates by Moreau, Ranson's *Anatomy of the Nervous System* (1939) for an account of the finer neurohistological arrangement, and Kuntz's *Autonomic Nervous System* (1934) for a general anatomical, physiological, and pathological consideration of the involuntary nerves.

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Chapter IV

GENERAL PHYSIOLOGY

In the preceding chapter it has been pointed out that the autonomic nervous system innervates non-striated muscle and glands which are not under the voluntary control of the cerebral cortex. These comprise the iris, the lachrymal, sudatory, and digestive glands, the heart and blood vessels, as well as tubular viscera such as the bronchi, the gastrointestinal and genitourinary tracts. It should be remembered that each of these structures, as a rule, receives a dual innervation, in part from the cranial or sacral division of the parasympathetic system, in part from the thoracolumbar outflow of the sympathetic. The purpose of this chapter is to outline the function of these two systems in the living organism. This will be taken up from the viewpoint of the physiologist rather than from that of the surgeon. The practical application of this knowledge and the details that are of special use in the clinic have been reserved for later chapters.

I. Homeostasis

The first approach to this subject was made by Claude Bernard (1878), who pointed out that, unlike the cold-blooded animals, mammals are independent of the medium which surrounds them. The greater adaptability of the warm-blooded animals to life in different surroundings is due in great part to the more efficient regulation of their vegetative processes by the involuntary nervous system. Man, in common with other mammals, is separated from his surroundings by a thin layer of dead cells or a film of mucus and salt solution. Within these walls he maintains his fluid matrix in a remarkably constant state. It was the great French physiologist who saw that the constant preservation of this "milieu intérieur" was the determining fac-

tor of our free and independent life. This personal, individual climate, which we carry about with us, must not change if we are to continue in a state of health. For example, external cold, which forces insects and reptiles to hibernate, stimulates the sympathoadrenal system of birds and most mammals to resistance. It prevents loss of heat by radiation through constriction of the peripheral arteries and by erection of the feathers or hair; at the same time it increases the production of heat by raising the blood sugar and the oxidative processes of the body.

When a warm-blooded animal is faced with a deficiency of oxygen, either through severe exertion or because of an ascent to high altitudes, or through the action of a gas like carbon monoxide, the sympathoadrenal system comes to the rescue. The heart is made to pump more rapidly, the great splanchnic area where blood accumulates during digestion is emptied by vasoconstriction, and the blood shunted to essential structures. Finally, by contraction of the spleen, millions of stored red blood cells are mobilized to help carry a greater oxygen supply. Barcroft, Nisimaru, and Puri (1932) have shown that this is brought about in part by the major splanchnic nerves and also by the increase of adrenine in the circulating blood.

After prolonged periods of strenuous muscular exertion the body sugar may be greatly reduced and the liver dangerously depleted of its glycogen reserve. Should the blood sugar fall below 45 mgm. per cent, as a result of either prolonged fatigue or insulin shock, convulsions leading to coma and death might follow. Before such a dangerous state is reached the sympathoadrenal system comes to the rescue by withdrawing further stores of glycogen from the liver and, unless the reduction is overwhelming, the blood sugar is maintained at a safe level. These same autonomic mechanisms free the laboring muscles of an excess of lactic acid and thereby protect the body from acidosis. Another by-product, heat, which is produced in enormous quantities by muscular work, is eliminated by stimulation of the sweat glands and by dilatation of the peripheral vascular bed.

Of particular interest to the surgeon is the response of the sympathoadrenal system to combat the damages resulting from severe accidents or operations. Here a number of protective reactions come to the rescue. In case of hemorrhage generalized

peripheral vasoconstriction maintains blood flow through the vital organs. The tendency to asphyxia, acidosis, dehydration, and loss of body heat which follow general anesthesia and prolonged operations are all combated by the thoracolumbar division of the autonomic nervous system.

In connection with the activity of the sympathetic nervous system in conditions which bring about the clinical picture of shock, an observation of unusual interest has been reported by Freeman (1933). He has shown in animal experiments that prolonged activity of the sympathetic nervous system results in a decrease in volume of the circulating blood. This reaction appears to be associated with prolonged vasospasm and does not occur in the sympathectomized animal. Such a concept is of fundamental importance, because it points out that if an emergency is too severe or too long continued, the very factors which normally act to preserve the organism may lead to its dissolution.

Cannon (1932) has summed up these "interofective" reactions which come to the individual's aid in fear, anger, exhaustion, and disease in the following words: "The important features in this strategy are, first, an absorption of extra acid in the buffer substances of the blood; second, a prompt supply of extra oxygen to burn the nonvolatile lactic acid . . . to volatile carbonic acid, which can be rapidly discharged; and third, an acceleration of breathing so that carbon dioxide is driven away from and extra oxygen is drawn into the lungs. In short, the circulatory and respiratory mechanisms work at their maximal capacity. Once more the sympathicoadrenal * system steps in to save the fluid matrix from grave disturbance. The circulatory adjustments—constriction of the splanchnic vessels, acceleration of the heart, discharge of extra corpuscles from the spleen—are all made by means of the sympathicoadrenal system. And in addition, this system probably plays a rôle in facilitating the respiratory processes, for it can quickly and effectively cause dilatation of the bronchioles and thus reduce the frictional resistance to the to-and-fro movement of the respired air."

A great part of the work which has led to our present understanding of the physiology of the sympathetic nervous system

* In his earlier papers Professor Cannon used this unabridged spelling, which he has subsequently shortened to "sympathoadrenal," and recommended that we do likewise.

has been carried out by Professor Cannon during the past thirty years at the Harvard Medical School. Working first on the reaction of the body to fear, rage, etc. (1929*A*, 1932), he came gradually to the appreciation of the wider importance of this system in adapting every adjustment of the body to the difficult situations which constantly confront us. One of his greatest contributions to this subject includes his observations on animals which have been totally deprived of sympathetic activity by removing the paravertebral ganglia from the neck to the lower lumbar regions (Cannon et al., 1929). These animals (cats) have lived in the sheltered conditions of the laboratory in good health for years. The animals become very sensitive to cold, as they have lost the ability to conserve heat. Erection of the hairs is permanently lost, but the peripheral arteries recover a degree of local vasomotor tone. Ability to perform muscular work and to resist fatigue is greatly reduced. These animals show no tendency toward vagotonia, as digestion is unchanged, the heart rate is only slightly slowed, and the blood pressure remains little altered. The basal metabolic rate is reduced about 10 per cent. The cat becomes pregnant and reproduces in a normal manner, but is unable to nurse her young (Cannon and Bright, 1931). There are no noticeable growth changes in kittens which have had a total sympathectomy performed on one side. This shows that the sympathetic nervous system is relatively unimportant in a protected constant environment, but emphasizes its essential character in the conditions of stress and strain which are met in normal existence.

In summing up the rôle of the thoracolumbar division, we should think of it as an emergency protective mechanism, which may not be functioning all the time, but which is always ready to go into action to combat any variety of adverse circumstance. Some of the most common conditions which arouse its activity are pain, extremes of temperature, asphyxia, hemorrhage, infection, dehydration, and hypoglycemia. Furthermore, any form of intense emotion or psychic trauma may stimulate a generalized sympathoadrenal discharge. Cannon (1933) has emphasized the interesting fact that this mechanism may actually be harmful unless the emotion is transformed into action. "If no action succeeds the excitement and the emotional stress—even worry or anxiety—persists, then the bodily changes due to the stress are

not a preparatory safeguard . . . but may be in themselves profoundly upsetting to the organism as a whole." Little attention has been paid to this effect by the medical profession, although it is of profound importance in human psychology. An understanding of the manner in which our involuntary nervous system reacts demands that we either permit our excitement to find appropriate expression without repression or learn to take an objective attitude which will counteract its deleterious effects. If the emotion cannot be controlled, Cannon suggests that the best thing to do is to work off the bodily changes which have occurred by hard physical exercise. In this way, if it is a matter of a temporary emotional upset, the body may be restored to normal. This same point has been aptly expressed by Fulton (1936*A*) in the statement that "the heart and circulation may be worked just as hard, and just as much as a detriment to the body as a whole, from an arm chair . . . as from a rower's seat." The deleterious effects which can be produced when the cortex loses its control over the more primitive autonomic centers in persons who are victims of nervous exhaustion or degenerative disease have been recently emphasized by Alvarez (1940).

Since the functions of the sympathetic nerves are catabolic and give rise to an extraordinary liberation of body energy, they are of a spendthrift character. Of equal importance to the body are the anabolic functions of the craniosacral (parasympathetic) division which come into play during the periods of rest and recuperation and are of a conservative character. In summing up their activity we shall again make extensive use of Cannon's excellent exposition in *The Wisdom of the Body*. The functions of the cranial division are carried out by a group of reflexes, conservative, protective, and up-building in their service. By narrowing the pupil the retina is protected from excessive light. By providing for the flow of saliva and gastric juice, and by increasing the tonic state of the gastrointestinal canal, proper digestion, absorption, and elimination of food substances are assured. Further evidence of the conservative influence of cranial autonomic tone is seen in the provision for rest and recuperation of the cardiac muscle by vagal slowing of the heart rate.

The function of the sacral division is in the main to empty hollow organs which are periodically filled. Sacral autonomic impulses cause contraction of the lower colon, rectum, and urinary

bladder. At the same time the involuntary sphincters of these reservoirs are relaxed. While less is known concerning the functional innervation of the reproductive tracts, it is known that engorgement and erection of the penis, together with the sensation of orgasm, are mediated by parasympathetic fibers over the nervi erigentes. The discharge of semen and the subsequent vasoconstriction are brought about by the opposing sympathetic impulses which traverse the superior hypogastric plexus. Simeone (1933) has shown that these fibers play an additional rôle in promoting peristalsis along the vasa deferentia. Resection of this plexus therefore results in sterility in the male, by preventing both the passage of spermatozoa to the seminal vesicles and their ejaculation during coitus.

It is apparent that these two great systems, which control the activity *of our circulatory, respiratory, digestive, and genitourinary* systems, are in a state of balanced opposition. Like the balanced tone of the extensor and flexor groups of muscles described by Sherrington, when one is excited, the other is inhibited. While the effect of the sympathetic impulses is very diffuse, the opposed effect of the parasympathetic is more specific.* Between the two every type of response, both general and local, is provided for. As Cannon puts it, "all the viscera can be influenced simultaneously in one direction or the other by varying, up or down, the . . . tonic activity of the sympathetic division. *And any special viscus can be separately influenced* . . . by varying . . . the tonic activity of the special nerve of the opposed cranial or sacral division that reaches directly to the viscus. Thus the heart may beat rapidly because the effect is part of the total complex of effects on the viscera produced by the sympathetic in emotional excitement; . . . or it may beat rapidly without extensive involvement of other viscera because of a *lessening of vagal inhibition.* The sympathetic is like the loud and soft pedals, modulating all the notes together; the cranial and sacral innervations are like the separate keys. When we consider that in emergencies the sympathetic functions in a great variety of ways to serve the organism as a whole, the importance

* See Chapter III. It has been shown that the preganglionic sympathetic [illegible] celiac ganglia, to synapse with a large num- [illegible] are widely distributed. In contrast to this [illegible] the viscera directly and synapse in the terminal plexuses with much shorter and more circumscribed postganglionic fibers.

of its arrangement for simultaneous and unified action becomes evident."

This coördination of the body as a whole to meet changing conditions in its external or internal environment by autonomic adjustments has been called "homeostasis" by Cannon (1929*B*). Homeostasis frees the individual from the difficult task of paying routine attention to the management of the details of bare existence. Without homeostatic control the warm-blooded animal would be in constant danger of disaster, unless always on the alert to correct voluntarily what the vegetative system regulates in a purely automatic fashion. With advancing age the nervous mechanism for the control of homeostasis becomes less efficient. Lasch and Muller-Deham (1930) find that a maintained vagus activity and diminished sympathetic activity cause a vagus preponderance in old age.

All automatic mechanisms, even the most efficient, may cease to function smoothly. The normally efficient homeostatic control may break down in certain abnormal conditions. For example, many individuals suffer from chronic vasoconstriction in the extremities; their hands and feet are constantly cold and moist from excessive perspiration. In other instances the heart may over-accelerate at the slightest stimulus, or food may fail to progress along the gastrointestinal canal at a normal rate. When these extreme reactions continue, they result in clinical syndromes such as Raynaud's disease, neurocirculatory asthenia, cardiospasm, and megacolon, as well as in a host of vague symptoms which cannot be classified under any definite diagnosis. Surgeons with a keen insight into the physiology of the autonomic nervous system have been able to devise methods of controlling a number of these abnormal states by paralyzing the nerves which bring them about.

II. Methods by which the Autonomic Nervous System Regulates Homeostasis

Autonomic Representation in the Cerebral Cortex. In the normal experiences of everyday existence disagreeable smells, tastes, sights, sounds, and emotions are a frequent cause of disturbances in the autonomic mechanisms. These upsets include such common effects as loss of appetite after tasting a bad egg or fainting at the sight of blood. These manifestations are due to

cortical reflexes mediated through connections with the lower autonomic centers in the hypothalamus.

Over sixty years ago, Hughlings Jackson (1876) suspected that visceral functions must have extensive representation in the cerebral cortex, since these functions are almost invariably disturbed during epileptic seizures. In the same year Eulenberg and Landois (1876) observed a rise in skin temperature of the contralateral extremities on ablation and a fall on stimulation of the motor-sensory area. From the clinic Gowers (1896) and Bechterew and Misslawsky (1886) have cited cases of hemiplegia and traumatic lesions near the "central gyrus" in man with increased temperature of the contralateral half of the body. The vasodilatation often persisted for a week or ten days and subsequently gave place to a colder, chronically paralyzed extremity. These early observations are in agreement with the recent findings of Ellis and Weiss (1936), who have investigated the circulation in a series of hemiplegic patients. But the problem is complicated by Kennard (1934) who cites physiological responses obtained from the premotor region (area 6 of Brodmann) in monkeys which were studied in Fulton's laboratory; in contrast to the findings of Eulenberg and Landois, she reports a fall of 2 to 4 degrees (Fahrenheit) in the contralateral extremities resulting from unilateral excision.* Fulton (1936*B*) attributes this cooling response on ablation of area 6 to the paralysis of the mechanism of reflex vasodilatation. In man Bucy (1935) has corroborated Kennard's findings on the basis of a number of clinical reports and observations of an instructive case. He concludes that vasoconstriction is often produced in cerebral hemiplegia through interruption of inhibitory impulses from the cortex to the vasoconstrictor centers of the hypothalamus and medulla. Our personal observations coincide with those first cited above. We would conclude that at the onset of hemiplegia the temperature of the skin is most often slightly elevated in the paralyzed extremities, whereas in cases of long standing the reverse is the case. However, we are forced to agree with Bucy that this material is too contradictory to be of value in elucidating the mechanism of central vasomotor control.

* This is in accord with the findings of Pinkston and Rioch (1938) in the monkey, but the exact opposite of Pinkston, Bard, and Rioch's (1934) earlier observations on the dog. Apparently species differences account for these confusing results.

More recent experimental stimulation of the cerebral hemispheres by Hoff and Green (1936) and Green and Hoff (1937) has disclosed a definite cortical influence on the lower autonomic centers. These investigators have concluded that "there is a mechanism by which the cortex (motor and premotor) can influence the state of the cardiovascular system, and that through this mechanism the cortex may bring about a finer adjustment of the activity of the heart and circulation in accordance with the exigencies of the external environment and the immediate activities of the skeletal musculature." In addition to cardiovascular effects, stimulation of the premotor area and certain adjacent parts of the cerebral cortex in monkeys has produced an increase of intestinal peristalsis, whereas bilateral extirpation has caused stasis and in several instances has been followed by intussusception (Watts and Fulton, 1934). Apparently there are no separate cortical areas for sympathetic and parasympathetic reactions, but the character of the reaction is dependent upon the general physiological state of the organism (Crouch and Thompson, 1939). In summing up present theories Fulton (1936*B*) states that "the coexistence in the same anatomical area of the cortex of autonomic and of somatic representation makes possible simultaneous and appropriate adjustments such, for example, as are necessary for heat regulation . . . Undoubtedly this overlapping also facilitates other cortically integrated reactions."

Autonomic Representation in the Cerebellum. The cerebellum, long considered the sole domain of somatic function, has recently been found to play a part in the regulation of respiratory and circulatory activity through its action on the autonomic centers in the underlying medulla. Moruzzi (1940) has shown that weak faradic stimulation of the paleocerebellar cortex (anterior lobe) causes strong inhibition not only of decerebrate rigidity, as is well known, but also of vasomotor reflexes and of the respiratory center. Connor (1941) has demonstrated, furthermore, that ablation of this area reduces the efficiency of thermal regulation.

The Central Ganglia in the Diencephalon. Recent investigations from many diverse angles have contributed to knowledge of the function of the central autonomic nuclei. To make the story of this research complete we must go back to the work of

Goltz forty years ago (1892). This showed that the decorticated dog is subject to manifestations of rage accompanied by signs of intense activity of the sympathetic nervous system. Dusser de Barenne (1919) made similar observations on cats, and Bard's (1939) extensive investigations have shown that the "sham rage" phenomenon is due to release of the sympathetic centers in the hypothalamus after removal of cortical inhibition. In 1909 Karplus and Kreidl began their investigation of the higher autonomic centers in the diencephalon by electrical stimulation of the walls of the third ventricle. Their investigations have been summarized by Karplus (1937). The position of the nuclear masses in this area has been established with a fair degree of accuracy (see p. 25) and much has been learned about their function by localized stimulation and destruction. This work has been facilitated by the Horsely-Clark stereotaxic instrument, and a number of excellent papers have appeared on the subject. The investigations of Ranson and his school, who have been the most assiduous workers, have been reviewed by Ranson and Magoun (1939). Another summary of outstanding interest, particularly of work in England, has been published by Beattie (1938). Further papers of special value by American investigators are collected in the research publications of the Association for Research in Nervous and Mental Disease (1940). The reader who is interested in this work can obtain a comprehensive review and an extensive bibliography from these sources.

For the purpose of this surgical monograph the rôle of the hypothalamic centers must be reviewed in a concise and rather dogmatic form. In brief, very clear evidence has been presented that stimulation of the paraventricular nuclei and the walls of the third ventricle more posteriorly results in a widespread discharge of the sympathetic division. Nearly all of the characteristic responses such as rise in blood pressure, cardiac acceleration, pupillary dilatation, erection of hairs, etc., have been produced by local stimulation of this area. Destruction of the same region has resulted in inability of animals to maintain their body temperature, but when the injury is more anteriorly situated, instead of poikilothermia there follows hyperthermia from inability of the organism to get rid of excess heat. Of pathological interest is the fact that Morgan and Vonderahe (1939) have found cellular degeneration in this exact area after death from

heat stroke. Posterior hypothalamic lesions in animals are often followed by striking somnolence. Ranson and Magoun (1939) have postulated that this region contains a "waking center." Corroborative evidence in favor of this theory has been brought forward by Serota (1939), who found that during the transition between wakefulness and sleep the local temperature and metabolism of this area are depressed. While the nuclear masses behind the optic chiasm give rise to a very vigorous sympathetic discharge, the results of stimulation and destruction more anteriorly give less definite responses on the part of the craniosacral outflow of the autonomic nervous system.

Evidence for parasympathetic representation within the hypothalamus was reported by Beattie (1932). On stimulating the lateral wall of the infundibulum under light barbital anesthesia he observed an increase in gastric peristalsis and secretion, hyperemia of the gastric mucosa, bradycardia, and increased peristalsis with a rise in bladder tone. Beattie, therefore, postulated that the preoptic region and anterior hypothalamus controlled the parasympathetic nervous system. Beattie and Sheehan (1934) also found pupillary constriction, fall in blood pressure, and rise in intragastric pressure with increased peristalsis of the stomach as a result of stimulation in this area. Stavraky (1936) was able to obtain in addition a dilatation of the pial arteries. Other workers, however, have been unable to confirm the existence of Beattie's parasympathetic center. Morison and Rioch (1937) concluded that a subcortical sympathetic inhibitory mechanism was located in the region of the anterior hypothalamus, but was in no sense comparable in effectiveness to the excitatory mechanisms of the posterior hypothalamus. As summarized by Ranson and Magoun (1939), stimulation of the preoptic area just in front of the optic chiasm and beneath the anterior commissure may cause contraction of the bladder, inhibition of respiration, and sometimes moderate falls in blood pressure; but it still remains to be determined whether this region can properly be regarded as a general parasympathetic center. This lack of a single center is not so surprising in view of the discrete nature of the parasympathetic discharge.

A third important function of the hypothalamus is the control of the pituitary gland. There is satisfactory proof that it controls secretion of the posterior lobe. This has been investigated by

Fisher, Ingram, and Ranson (1938) and the results of their experiments, together with the extensive literature on the subject, brought together in a monograph. By means of the supraoptico-hypophyseal tract the hypothalamus regulates the secretion of antidiuretic hormone from the pars nervosa of the pituitary. When either the nervous pathway or the posterior lobe is injured, polyuria results. This confirms and extends the theory, first promulgated by Hann (1918), that diabetes insipidus occurs in the absence of the neural division, if there is pars anterior tissue present.

Proof that anterior lobe secretion is regulated by the hypothalamus is far less impressive. The most convincing evidence is the work of Uotila (1939) on the activity of the thyroid during exposure to cold. Under these circumstances there is increase of thyroid secretion which is mediated by the thyrotropic hormone. This in turn appears to be stimulated by impulses transmitted from the hypothalamus through the pituitary stalk, because it fails to occur after stalk transection.

Cleveland and Davis (1936) have also shown that the hypothalamus may influence the secretion of diabetic hormone from the anterior pituitary. These investigators report that bilateral lesions of the tuber cinereum at the level of the ventromedial hypothalamic nuclei may be followed by pancreatectomy without the development of hyperglycemia and glycosuria. Such animals also become hypersensitive to insulin. In other words, injury to hypothalamic centers seems to produce the same effect as removal of the anterior lobe of the pituitary.

Responses observed in the course of operations on the third ventricle in man have been reported by one of us (White, 1940) and confirm the conclusions which have been derived from animal experiments. In the course of opening the lamina terminalis (the anterior wall of the third ventricle) for drainage of hydrocephalus in 5 adult patients under local anesthesia, it was possible to observe the effects of electrical stimulation of the region of the paraventricular nuclei. In each case there was a sudden and dramatic acceleration of the heart and rise in blood pressure (Fig. 22). The maximum acceleration of the pulse was from a basal rate of 55 to 145 beats per minute, with an elevation in systolic blood pressure of 20 mm. The change occurred after a latent period of 2 seconds and lasted for 2 minutes after the

current was cut off. As in experimental animals, electrical stimulation in the preoptic region was less effective in eliciting a parasympathetic response. A slowing of the heart from 52 to 45

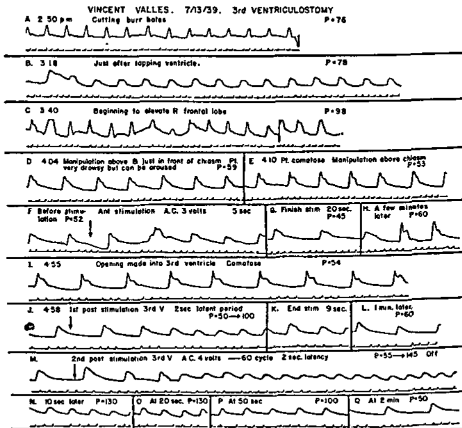


FIG 22. Changes in heart rate and blood pressure which accompany stimulation of hypothalamic nuclei in man.

D. and E. Operative manipulation above optic chiasm
F. and G. Electrical stimulation in region of anterior commissure.
J. and M. Electrical stimulation of lateral wall of third ventricle in region of paraventricular nucleus.

(Reproduced from White, 1940, courtesy of Association for Research in Nervous and Mental Disease)

is shown in Figure 22, but even this slight degree of bradycardia was not consistently obtained.* On the other hand, operative manipulation of the anterior hypothalamus consistently produced a sudden reflex bradycardia with a maximum slowing of the

* It is quite possible that a more definite bradycardia could be obtained on electrical stimulation, were it not for the extreme slowing already induced by operative manipulation of the anterior hypothalamus. Reflex slowing on manipulation above the chiasm does not occur when atropine and ether anesthesia are used.

heart from an initial rate of 175 to 70 beats per minute. Loud gastric peristalsis, nausea, and vomiting occurred in one instance, and abrupt loss of consciousness in 4 of 8 patients. Similar observations have often been made in the course of operative manipulation in this area (Dott, 1938).

In addition to these direct observations on the human hypothalamus, there are numerous clinical observations which point in the same direction. Tumors and other lesions which compress or destroy the walls of the third ventricle frequently destroy the heat regulating mechanism (Peet and Kahn, 1936; Alpers, 1936; Davison, 1940). One of the patients reported by Peet and Kahn with a hypothalamic tumor developed severe vasoconstriction with cyanosis and sweating of the extremities simulating Raynaud's syndrome. Other sequelae which have been observed in man include psychic changes (Gagel, 1936; Alpers, 1940), abnormal somnolence (von Economo, 1926, 1930; and Globus, 1940), and diabetes insipidus (Bailey, 1940). In the case of a pedunculated tumor in the third ventricle reported by Penfield (1929), extraordinary outbursts of autonomic activity appeared in repeated attacks. These manifestations consisted of cutaneous vasodilatation, salivation, sweating, and pilomotor activity. Tears flowed from both eyes, the pupils dilated, and in severe attacks the eyeballs protruded. The heart beat became strong and rapid, while the respiration was slowed. Following an attack the woman became constipated and experienced difficulty in emptying her bladder. She finally died after a prolonged series of attacks. Postmortem examination revealed a cholesteatoma of the choroid plexus which protruded into the foramina of Monro, causing an internal hydrocephalus. A second and closely similar case, resulting from an astroblastoma which arose from the floor of the third ventricle, has been reported by McLean (1934).

Alvarez (1940), who has made a long study of the complaints of nervous individuals, points out that many of their symptoms are in reality disconcerting tricks played on the heart, blood vessels, digestive tract, kidneys, and skin by an over-irritable involuntary nervous system. In health visceral function is regulated so well by the autonomic nuclei in the hypothalamus that the normal individual is nearly unconscious of his internal organs. As Bard's work (1939) has shown, this regulating center is normally kept in check by the cerebral cortex, but when upset in

any way it may work erratically and thereby cause disagreeable symptoms in many organs of the body, viz., palpitation, vasomotor disturbances, insomnia, and many varieties of gastrointestinal disorders, endocrine dysfunction, etc. Alvarez presents convincing evidence that the hypothalamus can be upset by fatigue, lack of sleep, or nervous strain; that in many persons it behaves erratically because of bad nervous inheritance; and that it may also be injured by an encephalitic virus or in older persons by little thromboses due to arteriosclerosis. Further investigation of disturbances during abnormal hypothalamic activity in states of nervous fatigue and in the psychoneuroses is urgently needed.

In summary, the hypothalamus, in addition to carrying out the expression of emotion, serves as a regulator of body temperature, the sleep-waking rhythm, and the whole delicate involuntary adjustment to the external environment. Through its influences on the pituitary body, as yet but poorly understood, it enters into the control of the endocrine system. In addition, through its nervous connections with the cerebral cortex and the thalamus, it is the recipient of those vague and indefinable stimuli which arise in association with all sorts of visceral activities and metabolic processes. In this way it mediates the integration of visceral and psychic impulses, and plays an essential part in the control of the internal milieu of the organism.

Autonomic Centers in the Medulla Oblongata. While the highest regulatory centers lie in the diencephalon, other important reflex centers governing vegetative processes are situated in the medulla. The important autonomic nuclei which contribute fibers to the cranial nerves are shown in Figure 6. As has been pointed out in Chapter III, the respiratory and vasomotor centers are closely associated with the dorsal motor nucleus of the vagus. It has long been known that when the brain stem is gradually sliced away, no fall in blood pressure is produced until the middle of the pons is transected, and that lower sections result in still greater drops in blood pressure until a point is reached just above the lower end of the fourth ventricle. No more exact delimitation of this area was made until the investigation of Ranson and Billingsley (1916). Their stimulation experiments suggest that there is a vasopressor center at the apex of the ala cinera or the fovea inferior and a depressor point slightly caudal to this (in the area postrema just lateral to the obex). Regard-

less of whether there are separate vasoconstrictor and vasodilator centers, it is certain that a well localized bulbar area controls the sympathetic outflow to the arterioles and that its tonic activity may be increased or decreased by afferent nerve impulses or by variations in the blood supply (Bard, 1929).

Another important area in the medulla which is situated more deeply in the reticular formation controls the rate and depth of respiration. This also has been divided into two opposed centers by Pitts, Magoun, and Ranson (1939). Stimulation of the more caudal area, which overlies the cephalic four-fifths of the inferior olive, results in maximum inspiratory movements of the thorax and diaphragm. Cupped over the cephalic end of the inspiratory area is a region from which expiratory movements are obtained. Figures presented by Finley (1931) showing lesions in the medulla in 2 cases of respiratory failure indicate that this localization of the respiratory centers in the cat may be applied roughly to man.

It was formerly supposed that nuclei in the medulla exert an important influence on the metabolism and heart-regulating mechanisms, but recent work has placed these centers at higher levels in the brain. Claude Bernard (1852) produced glycosuria by his classical puncture of the floor of the fourth ventricle, but the probable explanation of this effect is that he injured conduction pathways from the hypothalamus. There is evidence that carbohydrate metabolism is governed by the pituitary diencephalic mechanism (see p. 73), and it is most likely that the general metabolic control of the body is also situated in the higher centers of the diencephalon.

Autonomic Centers in the Spinal Cord. As described at the beginning of this chapter, the character of the autonomic functions, as well as the anatomical arrangement of the sympathetic nerves, necessitates a widespread distribution of their discharge. In spite of this, the nerve supply of the individual organs is given off from quite localized areas in the thoracolumbar and sacral regions of the spinal cord. Present knowledge of segmental spinal levels is summarized in Table I.

Subsidiary Reflex Centers That Modify the Activity of the Autonomic Nervous System.

a. The Carotid Sinus Mechanism. An important secondary mechanism which controls cardiovascular and respiratory ac-

TABLE I. THE SEGMENTAL MOTOR INNERVATION OF THE VISCERA

Organ	*Segments Which Give Off Parasympathetic Neurons*			*Segments Which Give Off Sympathetic Neurons*													
				Thoracic												Lumbar	
	Higher Cranial Segments	Vagus Nerve	2nd to 4th Sacral Nerves	1	2	3	4	5	6	7	8	9	10	11	12	1	2
Eyes	+			+	+												
Salivary Glands	+			+	+												
Blood Vessels of Meninges and Brain	+			+	+												
Blood Vessels of Head and Neck				?	+	+	+	+									
Sweat Glands of Head	+				+	+	+	+									
Blood Vessels, Sweat Glands, and Erector Pilae Muscles of Arms					+	+	+	+	+	+	+						
Heart		+		+	+	+	+	?									
Lungs		+			+	+	+	+	+	+							
Esophagus, *Stomach*, *Liver*, *Pancreas*, and Small Intestine		+						+	+	+	+	+	+	+			
Adrenal													?	+	+	+	?
Kidney		?												?	+	+	?
Bladder			+													+	+
Genitalia			+													+	+
Colon and Rectum			+													+	+
Blood Vessels, Sweat Glands, and Erector Pilae Muscles of Legs														+	+	+	+

tivity has been recently brought to the fore by the work of Hering and of Heymans and his collaborators in Ghent. They point out that there is a peculiar innervation of the region in which the common carotid divides into its internal and external branches; from this bifurcation a number of afferent rami are given off to the vagus and glossopharyngeal nerves. Stimulation of these fibers gives rise to far-reaching reflex responses (Fig. 15). The following summary of this work has appeared in a monograph by Heymans, Bouckaert, and Regniers (1933).

Carotid sinus regulation of blood pressure: At normal arterial pressure, variations of tension of only 10 to 20 mm. of water in the carotid sinus produce marked fluctuations in general systemic blood pressure. When the carotid sinus pressure is raised, the systemic pressure falls. At pressures above 200 mm. and below 50 mm. of mercury, reflex control of vasomotor tone disappears. The authors have demonstrated that within these limits a rise in carotid pressure will produce peripheral vasodilatation and a fall in general systemic blood pressure. There is also an increase in the size of the spleen and of the intestines, together with a diminution in rate of blood flow and an increase in cardiac volume.

Reflex regulation of the heart and lungs by the carotid sinus: Heymans has also shown that the carotid sinus exerts an important reflex control on the activity of the heart and lungs. Perfusing the carotid sinus with blood containing varying concentrations of carbon dioxide and other weak acids causes characteristic acceleration of respiration, even though the blood flowing through the brain is unaltered. In the case of the heart, marked changes in its rate and the force of its beat can be produced by perfusing the isolated carotid sinus with adrenaline.

Bronk (1931) has further elaborated Heymans' studies. By using a vacuum-tube amplifier and an oscillograph attached to the carotid sinus nerve, he has been able to show a burst of nerve impulses accompanying each heart cycle. This discharge is coincident with the rapid rise in arterial pressure revealed by the carotid pulse curve. At high blood pressures this discharge becomes continuous, an effect which is also produced as the result of asphyxia. The general character of these discharges from the carotid sinus agrees closely with those found in the cardiac depressor nerve. The activity of the senory nerve endings in both areas appears to constitute an important mechanism in prevent-

ing excessively high blood pressures or dangerously rapid heart rates.

b. The Cardiovascular Depressor Mechanism in the Aortic Arch. Still another secondary mechanism for the control of the heart and blood vessels lies in the sensory network in the arch of the aorta. From this plexus impulses reach the higher cardiovascular centers over the depressor branch of the vagus, the "nerve of Cyon and Ludwig" (1866). These afferent impulses set up cardio-inhibitory and vasodilator responses and protect the organism from sudden and dangerous periods of hypertension. Like the carotid sinus mechanism, the sensory zone in the aortic arch modifies the general activity of the autonomic system in a reflex manner.

Axon Reflexes. The lowest level at which segmental adjustments of general visceral activity take place lies in the sympathetic ganglia. Although anatomical evidence is lacking to show synapses between visceral afferent and motor neurons outside the spinal cord, some physiological evidence exists that reflex actions may, under certain circumstances, be carried out through the sympathetic ganglia (Kuntz, 1934, 1940). Sokownin (1874) first observed this response in the inferior mesenteric ganglion. After severing all central connections, stimulation of the central end of one hypogastric nerve resulted in contraction of the bladder from an efferent impulse descending the other nerve. Langley and Anderson (1894) reproduced this response and observed at the same time a contraction of the internal anal sphincter and blanching of the mucous membrane of the rectum. These reflexes were blocked by nicotine applied to the inferior mesenteric ganglia. Since these reactions were unlike the ordinary spinal reflexes, Langley (1900) called them pseudo or axon reflexes. He also noted that reflex impulses traversing a preganglionic neuron usually spread over three to four segments, whereas a postganglionic reflex, carried out through a single axon and its branches, called forth a response limited to its own proper distribution. The whole subject of axon reflexes is somewhat obscure and should be reinvestigated with modern physiological methods.

III. Visceral Responses to Autonomic Stimuli

Vasoconstriction. In addition to distributing vasoconstrictor fibers to the entire surface of the body, the sympathetic system

constricts the cerebral and retinal arteries, as well as the great vascular network to the splanchnic and pelvic viscera. Since the capacity of the vascular bed is greater than the total volume of the blood, active vasoconstriction must be in force over large areas to insure an adequate circulation to the vital organs. When an unusual demand for blood arises in a given territory, it may be met either by a relaxation of vasoconstrictor tone or by active vasodilatation. As the problem of modifying deficient circulation in the extremities is of primary concern to the surgeon, this phase of vasomotor physiology requires particular emphasis.

The most common vasoconstrictor stimulus is cold. As Maddock and Coller (1933) have pointed out, vasomotor reactions are most intense in the extremities. The arms and legs comprise 65 per cent of the body surface and, by their efficient vasomotor responses, regulate in major part the elimination or storage of body heat. Under such conditions as pain, fear, anger, asphyxia, hemorrhage, and dehydration vasoconstriction in the extremities may become so intense that the cutaneous circulation nearly comes to a standstill. In certain abnormal states chronic vasospasm may persist in normal surroundings and produce a degree of stasis in the terminal arterioles that causes color changes, pain, and eventually trophic disturbances. Attempts to relieve vasospasm by section of the vasoconstrictor nerves constitute one of the most interesting chapters in the field of sympathetic neurosurgery.

Knowledge of the segmental level of the vasoconstrictor outflow has been worked out by animal experiments and observations on man. Budge (1853) discovered that hemisection of the cord at the last cervical segment resulted in a striking increase in temperature of the rabbit's ear on the operated side. Edes (1869) later observed that the vasomotor fibers to the arm leave the spinal cord as low down as the sixth thoracic segment. According to Langley's well-known findings (1892), which were derived from stimulating the motor roots within the spinal canal, vasoconstrictor, as well as sudomotor and pilomotor, impulses to the arm are given off from the fourth to tenth thoracic segments. In analyzing these findings with the advantage of more recently acquired knowledge, it is evident that higher segments give off vasoconstrictor fibers to the arm. Sheehan and Marrazzi (1941) have recently repeated Langley's experiment, using the cathode

ray oscillograph to detect sympathetic impulses in the peripheral nerves of the arm and leg. With this sensitive indicator they have found that the fourth to eighth thoracic segments contribute sympathetic fibers to the arm. This work was done on monkeys. In man an even greater number of segments contribute vasoconstrictor and sudomotor fibers. Foerster (1939) has stimulated ventral spinal roots on the operating table and made the following observations: Stimulation of the first and second thoracic *motor roots produced vasoconstriction of the ipsilateral face and* neck, but no vasomotor changes in the arm; stimulation of the third to seventh ventral roots caused plethysmographic evidence of vasoconstriction in the upper extremity. Postoperative tests performed in this hospital have shown unequivocally that when the sympathetic chain is cut below the third thoracic ganglion, vasoconstriction and sweating persist in the head and upper extremity. But when, in addition to section of the sympathetic trunk below its third thoracic ganglion, the second and third intercostal nerves are divided proximal to their sympathetic rami, these functions are abolished. Notwithstanding a statement of Kuntz, Alexander, and Furcolo (1938), we have never been able to find evidence of the presence of any vasoconstrictor or sudomotor fibers in the first thoracic nerve (see Chap. VIII).

Langley (1891*A* and *B*) also studied the sympathetic outflow to the hind limbs of the cat and concluded that these impulses originate from the eleventh thoracic to second lumbar levels. Sheehan and Marrazzi (1941) have found that in the monkey fibers arise from the twelfth thoracic to third lumbar segments. This corresponds in man with the eleventh thoracic to second lumbar roots, which appears to be correct from surgical experience.

While the most active vasoconstrictor action takes place in the arterioles, a definite nervous control of the capillaries and veins has also been demonstrated. Beecher (1936), working in Krogh's laboratory, studied the capillaries in the rabbit's ear with the Clark window technic. He observed that cessation of flow through the capillary loop results from constriction of the Rouget cells and swelling of the endothelial cell nuclei. This reaction follows disagreeable stimuli within a second, too short a latent period for anything but nervous action.

Evidence that the veins are also under the control of the

nervous system has been summarized in McDowall, Malcolmson and McWhan's (1938) monograph on the control of the circulation. They cite the experiments of Gollwitzer-Meier and Bohn (1930), who found that the mesenteric veins of dogs, when connected to the animal only by the nerves, are constricted when carbon dioxide is inhaled. There is further evidence that venous tone can be increased or inhibited reflexly as the result of pressure changes in the carotid sinus. The fact that the veins become engorged after sympathectomy is therefore not entirely due to the "vis a tergo" of an increased blood flow through the capillaries, but is in part due to their release from the vasoconstrictor center.

Vasodilatation. Although a concise knowledge of the vasodilator mechanism is still lacking, it is known that vascular relaxation can be brought about both by sympathetic and parasympathetic impulses. Dale's (1906) discovery that adrenaline, after paralysis of the sympathetic constrictor endings by ergotoxine, causes a fall instead of a rise in pressure is perhaps the best evidence for a separate system of sympathetic vasodilator nerves. A striking clinical proof of the presence of sympathetic dilator fibers is the diminished ability of sympathectomized peripheral arteries to dilate in response to body heating (see p. 84 below). To complicate a difficult problem further, there is evidence that the sympathetic system contains both adrenergic and cholinergic vasodilators. The arguments, of course, are extremely complex and do not properly belong in a clinical discussion of this subject. The reader who is interested in examining the conflicting views on this problem should consult the recent review by Burn (1938).

In certain special tissues the usual vasoconstrictor rôle of the sympathetic fibers is reversed and the reaction to their discharge as well as the reaction to adrenaline is vasodilatation. This appears to be the case with the coronary (see p. 277) and pulmonary * arteries, as well as with the circulation to skeletal muscle (see next section).

It has long been recognized that parasympathetic dilator fibers run to the upper abdominal viscera in the vagus and to the pelvic organs in the sacral nerves. Parasympathetic dilator fibers also run in the sensory portion of the facial (nervus intermedius of

* For the lung this has been conclusively established only in cold-blooded animals.

Wrisberg) to the lachrymal and salivary glands (p. 260), to the tongue (p. 261), and to the cerebral vessels (p. 255).

Considerable obscurity still persists concerning the anatomical distribution of the vasodilator fibers to the peripheral vascular system. Stricker (1877) first demonstrated flushing in the extremities by stimulating the distal ends of the divided posterior spinal nerve roots. Bayliss (1901), who repeated Stricker's experiments, found that these fibers do not join the sympathetic chains and do not degenerate when the posterior roots are cut. Hence he concluded that their trophic cells must lie in the sensory root ganglia and that the vasodilator fibers are, in fact, identical with the sensory afferent neurons. Consequently he postulated an "antidromic" type of conduction which necessitates the assumption that the sensory neurons may transmit impulses in a direction contrary to that stipulated in the Bell-Magendie Law. A heated discussion has arisen over the problem whether the vasodilator action of the posterior roots may be transmitted over a special set of efferent fibers (Foerster, 1928; Kuré, 1931; Barron and Matthews, 1935; Sheehan, 1935; Okelberry, 1935), or whether the intact fibers which have been observed in the central stumps of cut posterior roots represent regenerating axons which have bridged the gap between the severed root endings by regeneration from the distal stump (Ranson, 1914; Hinsey, 1934; Westbrook and Tower, 1940). Sheehan (1935) summarized the status of this difficult problem by saying that it "unfortunately does not allow of a final histological solution, as the times for regeneration and degeneration overlap, and it is almost impossible to fix an arbitrary time at which one can be sure that all requisite degeneration has taken place and no regeneration has occurred." It is possible, as Sheehan has suggested, that vasodilatation is mediated over posterior roots by a special set of fibers with their cell bodies in the root ganglia, and that they are ordinarily stimulated through afferent impulses over the sensory fibers as a form of axon reflex. After evaluating the evidence given above we have been forced to conclude that it is most unlikely that the cell bodies of these fibers lie in the spinal cord and that there is no reason whatever to believe that they belong to the parasympathetic system, as was proposed by Kuré (1931).

In the extremities the posterior root fibers are not the sole vasodilator pathway. Lewis and Pickering (1931) have pointed

out that sympathetic ganglionectomy destroys the power of the peripheral arteries to dilate, as well as to constrict. Figure 23 shows the loss of vasodilator response in the sympathectomized hand when the body is heated. It is the smooth muscle cells innervated by this system of sympathetic vasodilator nerves which must be affected by adrenaline after the constrictor mechanism

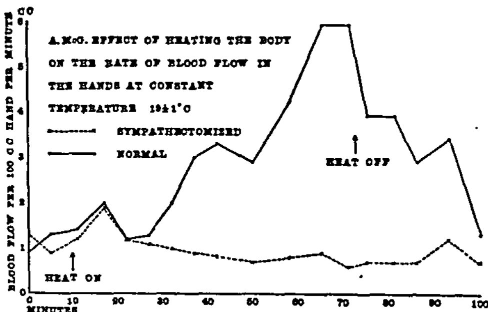


Fig. 23. Vasodilator response to body heating abolished by sympathetic ganglionectomy.

Measurements of blood flow were made by Dr. N. E. Freeman by his plethysmographic method. While the hands were in water at a constant temperature of 19°C (66°F.), the patient was exposed to a heat of 50°C. (122°F.).

has been paralyzed by ergotoxine. From available evidence it appears that the sympathetic vasodilator pathway is the more important in temperature control, and that the posterior root dilators are active only in certain special functions such as emotional flushing.

The only possible conclusion to be derived from these data is that both the sympathetic axons in the anterior roots and certain fibers in the posterior roots carry vasodilator impulses to the extremities. There is no evidence for a comparable duplication of vasodilator nerves to the viscera.

Vasomotor Responses in Skeletal Muscle. Present concepts of the physiological mechanism that controls the flow of blood in skeletal muscle are extremely confused, because of extraordinary

variations in different species of animals which have been used for investigation (Burn, 1938). In man Grant (1938) found that the local vascular effects of exercise are independent of the sympathetic nerves, and evidence points strongly to relatively stable metabolites as being responsible for the hyperemia of exercise. The action of nervous stimuli on the vascular bed of skeletal muscle has been extremely difficult to quantitate, but a fairly satisfactory approximation has been made by measuring volume changes in the extremities by a plethysmograph. This method, developed by Grant and Pearson (1938), compares the alterations in volume which occur in the hand or foot with those in the forearm and calf. In the more distal portions of the extremities, where the skin constitutes a large proportion of the total volume, the reaction to painful stimuli and to adrenaline is strongly vasoconstrictor. On the other hand, in the forearm and calf, where the greater bulk of tissue is composed of skeletal muscle, sensory stimuli have either no effect or produce vasodilatation. Small doses of adrenaline regularly cause an increase of limb volume, due to vasodilatation of voluntary muscle.* Furthermore, the vasodilator action of adrenaline is increased after sympathectomy. Although these observations require confirmation from more direct measurements of blood flow, they serve to indicate that the response of skeletal muscle to sympathetic impulses or sympathomimetic substances is one of increased circulation.

Piloerection. Erection of hairs diminishes radiation of body heat. It is solely under sympathetic control, there being no known parasympathetic inhibition. While this function is rudimentary in man, its distribution coincides with the nerve supply of the cutaneous vessels and sweat glands, and its loss is an important sign of sympathetic paralysis.

Sudomotor Activity. The neurophysiology of sweating has been investigated by Guttman and List (1928), and much further work has been reported in a recent series of papers by List and Peet (1938 *A*, *B*, *C*, *D*). Activity of the sweat glands is controlled by the autonomic nervous system and may be classified as (1) thermoregulatory, (2) emotional, (3) "drug-sweating," in-

* [illegible] is observed that adrenaline causes [illegible] muscles. He suggests that the [illegible] vessels causes dilatation of the [illegible]

duced by pilocarpine and mecholyl, and (4) the sweating of the face which is induced by gustatory stimulation. Sweating in response to heat or nervousness appears to be entirely under the control of the thoracolumbar division. As is shown in the following chapter, the postganglionic sympathetic fibers are as a rule adrenergic. In the case of the sweat glands, however, they are cholinergic in man.* As a result, the sweat glands are not affected by adrenaline, but are stimulated by acetylcholine and pilocarpine, even after sympathectomy. In the case of the head, List and Peet (1938*D*) have shown that sweating may be provoked by gustatory stimulation (chewing spicy foods) and appears around the lips and nose. This phenomenon is slight under normal circumstances, but may be greatly increased after degeneration of the postganglionic sympathetic sudomotor fibers. The explanation for this is given in the following chapter and its clinical applications are described in Chapter X.

Ocular Responses. Paralysis of the cervical sympathetic nerves has been described as producing a triple response: constriction of the pupil, drooping of the upper eyelid, and recession of the orbit. The constriction of the pupil was first observed by du Petit (1727), and the complete phenomenon in animals described a century and a half later by Claude Bernard (1852), and in man by Horner (1869) (see Fulton, 1929). Not altogether logically, therefore, it has come to be known as Horner's syndrome. In the control of the iris the opposed innervation of the cranial autonomic and the sympathetic are clear cut, the former producing pupillary constriction, the latter dilatation. Recent studies have shown that the other two features that make up the classical triad require modification. There is not only a drooping of the upper eyelid, but also a distinct elevation of the lower. The enophthalmos, which is definite in animals, is nothing more than an optical illusion in man, due to the narrowed palpebral fissure. Müller's muscle, which protrudes the orbit in animals, is not developed in man, and recent measurements with the exophthalmometer by Mutch (1936) and Pochin (1939) have shown that there is no actual protrusion or recession of the human eyeball during stimulation or paralysis of the cervical sympathetic fibers. Further clinical changes associated with this phenomenon are described in Chapter X (p. 262).

* In some other species, the horse, for example, they are adrenergic.

Salivation. Both systems of nerves stimulate the secretion of saliva. Heidenhain (1868), who first investigated the neurogenic control of salivary secretion, showed that in the dog weak faradic stimulation of the chorda tympani nerve causes vasodilatation as well as an increased secretion in the submaxillary and sublingual glands. Stimulation of the cervical sympathetic also causes a slight amount of secretion, but this is thirty to sixty times less than the amount obtained from a discharge of corresponding intensity over the chorda tympani. At the same time the glands show distinct vasoconstriction. Langley (1878) observed that when both the chorda tympani and cervical sympathetic nerves were stimulated, he obtained a more copious secretion than by stimulation of either nerve separately. These experiments show that autonomic impulses influence the flow of saliva by stimulating the secretory cells as well as by altering blood flow through the glands. From a clinical viewpoint it is fair to postulate that the cranial autonomic is the system chiefly responsible for salivary secretion.

Thyroid Secretion. This much disputed subject has been reviewed by Means (1937). From the fact that Cannon, Binger, and Fitz (1915) succeeded in producing a syndrome very much like exophthalmic goiter in cats by anastomosing the phrenic nerve with the cervical sympathetic, it seemed at first as though thyroid secretion was stimulated by nerve impulses. But Friedgood and Cannon (1940) on the basis of more recent work have concluded that this stimulation is probably a hormonal one secondary to stimulation of the anterior pituitary. Nonidez (1935), who has made the most careful study of thyroid innervation, draws the conclusion that there is no true secretory innervation, but that the gland's very complex vasomotor nerves may regulate the escape of hormone in the blood and may perhaps govern its production by regulation of the oxygen supply.

Neurogenic Control of the Thoracic Viscera. The antagonistic action between the sympathetic and parasympathetic systems is well exemplified in the response of the heart. Sympathetic stimulation increases the activity of the cardiac musculature, resulting in an acceleration of the heart beat and an increase in stroke output. In contrast to its general vasoconstrictor action, the sympathetic dilates the coronary arteries to supply the laboring heart muscle with an adequate flow of blood (Anrep and

Segall, 1926; Gollwitzer-Meier and Kruger, 1935).* The vagus produces opposite motor effects. It also transmits afferent impulses from the arch of the aorta which act on the cardiac and vasomotor centers in the medulla and bring about slowing of the heart rate and widespread vasodilator reflexes. In some animals and occasionally in man these fibers constitute a distinct branch (the depressor nerve of Cyon and Ludwig); but more commonly they ascend in the trunk of the vagus. The carotid sinus innervation is a further afferent reflex mechanism which serves to protect the heart from over-exertion.

In the lung it is known that vagal stimulation constricts the larger bronchi, as this response has been observed through the bronchoscope. Beyond this, little is known concerning the responses of the finer bronchioles. This state of uncertainty is due to the difficulties in measuring the volume of air or blood in a system with so many variables (see p. 347).

Little more has been conclusively proved concerning the vasomotor control of the pulmonary vessels. Bradford and Dean (1894) believed that their observations were an adequate demonstration of the existence of a vasomotor supply to the lungs, though they thought that this innervation was less well developed than that of the systemic vessels. A confused and contradictory literature has arisen since, but the balance of evidence is in favor of a weak vasomotor control. Hall (1923), by illuminating the surface of the lung, was able to study the behavior of the small vessels directly. He observed that the intravenous injection of adrenaline produced marked arteriolar constriction. Recent perfusion experiments on the isolated lung cited by Wright (1932) show that sympathetic stimulation causes definite vasoconstriction. DeBurgh Daly and von Euler (1932), who have made most carefully controlled experiments on lung innervation, found a rise in pulmonary artery pressure of 40 per cent on sympathetic stimulation. They also concluded that vasodilatation in the lung is probably due to vagal activity.

Neurogenic Control of the Digestive Tract.

a. *The Esophagus.* Knight (1934) has reviewed the theories of esophageal innervation. In addition he has presented interesting observations on the effect of stimulation or paralysis of the

* Not all investigators are in accord on this point, but we believe that the most satisfactory evidence favors this interpretation (see Chap. XI).

sympathetic and vagal branches to the esophagus. His experiments give clear-cut evidence that the vagus and splanchnic nerves exert an antagonistic influence on the tone of the esophageal musculature and its cardiac sphincter. In this dual mechanism, as in the case of the terminal gut, the parasympathetic stimulates peristalsis and opens the sphincter, whereas the sympathetic causes inhibition of peristalsis and constriction of the sphincter. Bilateral vagectomy in cats brought about a condition closely resembling cardiospasm in the human being. If allowed to continue, the animals died of obstruction, but if the sympathetic supply was divided by stripping the fibers surrounding the celiac axis, the condition of achalasia gave way to a patulous sphincter. Ferguson (1936) has produced cardiospasm in monkeys in the same way, but attempts to relieve this condition in man by sympathectomy have not met with consistent success.

b. The Gastrointestinal Canal. Evidence that stimulation of the posterolateral nuclei of the hypothalamus (sympathetic centers) inhibits gastrointestinal activity and that stimulation more anteriorly causes an increase in gastric peristalsis and acid secretion has been presented (see p. 72). Sheehan (1940) has written the most complete and up-to-date review of this subject and his article should be consulted by those who would seek further information and an extensive bibliography.

Although the smooth muscle of the stomach and small intestine, as well as the pyloric sphincter and the digestive glands, receives a dual innervation, separate stimulation of the splanchnic nerves or the vagi does not give any such clear-cut antagonistic response. It is possible that this failure of the usual opposed innervation of the parasympathetic and sympathetic divisions is apparent rather than real—due to their mixed anatomical composition (see p. 41).

The little that is definitely known concerning the influence of the extrinsic nerves on digestion has been summarized by Alvarez (1928). There are times when the central nervous system must communicate with the digestive tract. There are times also when different segments of the tract need to synchronize their activity. On such occasions the extrinsic nerves come into play. The vagi carry feelings of hunger and satiety from the stomach to the brain; they help in adjusting the tone of the

stomach to food coming down the esophagus (Cannon, 1911);* and they carry stimuli that give rise to the psychic secretion of gastric juice (Pavlov, 1910). Moreover, they probably carry messages from the digestive tract which makes the animal feel comfortable and sleepy (Loeb, 1900). The splanchnics serve largely to quiet the tract and to stop digestion when the body is distressed or injured (Cannon, 1909). The extrinsic nerves probably have much to do with digestive upsets associated with disease elsewhere in the body. Of interest in this connection are the studies of Walton, Moore, and Graham (1931) on the vomiting pathways of peritonitis. They have shown in dogs that both the vagus and the splanchnic nerves carry reflex stimuli which lead to vomiting and that both must be cut in order to prevent it.

Cannon (1933), in his excellent review of the physiology of digestion, pointed out that some of the incongruous results obtained by electrical stimulation of the vagi and splanchnic nerves can be explained as a consequence of what he so aptly called "induction coil physiology." In the intact animal or human being it is apparent during varying emotional states that the general autonomic influence on gastrointestinal activity follows the fundamental rules of homeostatic behavior. Periods of anger, fear, or worry result in complete depression of the digestive functions, while states of contentment and psychic stimulation at the sight or thought of food result in an active flow of gastric juice and a speeding up of the digestive processes. About a century ago the famous French philosopher and gourmet Brillat-Savarin (1839) described the psychic stimulation aroused in contemplating savory food. "Memory recalls foods that have flattered its taste: imagination fancies that it sees them . . . the whole nutritive apparatus is moved. The stomach becomes sensible, the gastric juices displace themselves with noise, the mouth becomes moist and all the digestive powers are under arms, like soldiers waiting the word of command. After a few moments there will be spasmodic motion, pain, and hunger." Indeed Alvarez (1929), from whom the preceding delightful quotation has been taken, cites another bon-vivant (whose anal sphincters had been destroyed by a series of operations for fistula) in whom

* In this connection we have a recent report of a patient with interesting physiological changes following total interruption of the vagal rami to the stomach. In addition to striking gastric stasis and atony, all sense of hunger has been lost (see p. 356, footnote.)

the sight, smell, or even the thought of food set up an uncontrollable defecation reflex. His rush waves of peristalsis were particularly annoying at breakfast, when his empty bowel was so sensitive that he had to eat seated on the toilet bowl.

The fact that the opposite disagreeable emotions can upset digestion has been recognized since the classical experiments of Beaumont (1833) on the fistulous stomach of Alexis St. Martin. He observed that violent passion was likely to cause a reflux of bile into the stomach, a change in the properties of the chyme, and a retardation of its passage onward into the intestine. It is common observation that the digestion of children is more easily upset by excitement or fatigue. Cannon cites the case of a refined and sensitive woman who came to her physician in Boston to be examined for digestive troubles. A gastric analysis on the following morning revealed a large amount of her supper of the previous evening still undigested. The explanation for this was not an obstructed pylorus, but a night of worry over an intoxicated husband. A subsequent gastric analysis, when the patient was no longer upset, showed a normally functioning stomach. Numerous other instances of this sort are reported in Alvarez's article. It is now generally recognized by physiologists that the effects of emotion on the digestive tract in animals can be largely interrupted by section of the vagus and splanchnic nerves, but that the essential mechanism of peristalsis that sweeps food along from mouth to anus is inherent in the intrinsic nerve plexuses of the gastrointestinal canal.

Many clinicians have pointed out the relationship between peptic ulcer and hyperactivity of the involuntary nervous system. In substantiation of this theory, Cushing (1932) and numerous other neurosurgeons have described acute perforating *ulcers in the human stomach coincident with tumor or operative* interference with the hypothalamus. In this connection, experimental hypothalamic injury in animals is followed by mucosal hemorrhage and ulceration in about one-third of all such experiments (Sheehan, 1940). While this work is suggestive, it should be pointed out that only acute ulcers have been produced in these experiments. Nothing resembling chronic peptic ulcers in man has been observed, and therefore we cannot yet accept these observations as proof of the neurogenic theory of formation of gastric and duodenal ulcer.

In the lower portion of the sigmoid and rectum the characteristic clear-cut antagonism between the sympathetic and the sacral autonomic nerves again becomes apparent. Gaskell (1916) showed that the smooth muscle of the internal anal sphincter was contracted by the lumbar sympathetic nerves. Learmonth and Markowitz (1929 and 1930) made pressure readings in the rectosigmoid, demonstrating an increase in pressure on paralyzing the lumbar sympathetic fibers, and a fall in pressure on stimulating these same fibers. Adamson and Aird (1932) have been able to produce megacolon experimentally in cats by resecting the sacral autonomic nerves. There is therefore evidence that the thoracolumbar sympathetic outflow causes a relaxation of the muscle in the wall of the sigmoid and rectum with a coincident constriction of the internal sphincter, i.e., an inhibition of the defecation reflex. The sacral parasympathetic innervation, on the other hand, produces exactly the reverse effect and thereby stimulates defecation.

c. Liver and Pancreas. Claude Bernard (1877), after his discovery that glycosuria and hyperglycemia resulted from the puncture of a certain region in the floor of the fourth ventricle (see p. 77), studied the conduction pathways from this area to the liver. Following section of the spinal cord in the lower thoracic region, glycosuria resulted as before, but cutting the upper thoracic cord abolished this response. More recent experiences (Kuntz, 1934) indicate that the sympathetic secretory fibers to the liver run in the fifth and sixth white communicant rami. Long (1940) has summarized the evidence in favor of a central nervous regulation of carbohydrate metabolism by the liver and pancreas. He cites the experimental work of Zunz and LaBarre (1928), which, although unconfirmed, lends basis to a rather attractive hypothesis of blood glucose regulation by the autonomic nervous system. This hypothesis postulates that the level of the blood glucose passing through the sensitive hypothalamic centers determines the activity of the glands concerned with carbohydrate metabolism. Thus, when the hypothalamic glucose level is elevated, insulin secretion is stimulated through the vagi. On the other hand, when the level falls, glucose is liberated from the liver by the combined activity of the adrenal medulla and hepatic nerves. No criticism can be found of the view that sympathetic impulses can elevate the blood sugar

level, but the relation of the vagi to insulin secretion is in Long's opinion more questionable. Until more convincing facts are established, it would seem that the major control of carbohydrate metabolism is to be found in the activity of the anterior pituitary, adrenal cortex, and islands of Langerhans. It is still quite possible that their activity is regulated directly by the composition of the blood passing through them.

There is also a certain amount of evidence that protein metabolism is mediated by autonomic impulses from the diencephalon. Freund and Grafe (1912) showed experimentally that it is augmented by the sympathetic and inhibited by the parasympathetic nerves. The secretion of bile, on the other hand, is stimulated, though only partially, by the vagus (Eiger, 1915).* The observations of Bainbridge and Dale (1905) show that the musculature of the biliary system responds in general to vagus and splanchnic stimuli much as does the musculature of the gastrointestinal tract.

The action of the extrinsic nerves on the digestive secretions of the pancreas is still not thoroughly settled. Although the secretion of water, bicarbonate, and the digestive enzymes in the pancreatic juice is stimulated in part by the action of "secretin" in the circulating blood, the digestive activity of the pancreas is also controlled by its autonomic nerves. Beginning in 1878 Pavlov observed that atropine inhibited pancreatic secretion. More recent experiments by his students show that the vagus nerves excite the pancreatic acini to secrete digestive juice. Mellanby (1926) has carried out the most complete studies on pancreatic secretion and found that as a result of vagus stimulation the trypsin and amylase in the pancreatic juice are increased, whereas the liquid and bicarbonate content remain unchanged. (The secretion of the latter he ascribes to the action of "secretin.")

Neurogenic Control of the Urinary Tract.

a. Kidney. Transplantation of the kidney, successfully performed by Carrel and Guthrie (1906) proved that the totally denervated kidney can carry on all functions which are essential to life. The earlier studies on renal denervation, notably those of Quinby (1916) and Marshall and Kolls (1919), indicated a

* Hillyard (1930) has shown that the most important stimulus to the secretion of bile is a chemical one.

temporary increase in urinary secretion. Nearly all investigators have agreed that denervation causes no change in the elimination of phenolsulphonephthalein, sodium chloride, lactose, urea, and many other substances. The most recent and carefully controlled experiments of Rhoads, Van Slyke, Hiller, and Alving (1934) on dogs showed no consistent effect on either the excretory efficiency of the kidney or on the renal blood flow. These results in animals have been confirmed in man by Page and Heuer (1935*A* and *B*). Measurements of urea clearance and volume of urine secreted from the normal and the denervated kidney (resection of nerve fibers in the renal pedicle) failed to show any significant difference over a period of months following operation.

The importance of the renal nerves has been still further minimized by a recent investigation of reflex inhibition of urinary secretion through afferent stimulation. Even after painful traumatic stimuli the reduced secretion of urine cannot be attributed directly to nervous inhibition or decrease in blood flow, because Theobald and Verney (1935) have found a similar inhibition of water diuresis in the completely denervated kidney. They have proved that this is not a response to circulating adrenaline, but probably is due to physiological variations in the activity of the posterior lobe of the pituitary. This is also probably responsible for the decrease in renal secretion during sleep.

b. Ureter. The ureteral nerves are known to carry afferent impulses, but subserve no known motor function. Experimental stimulation as well as the administration of adrenaline (Elliott, 1907) has failed to show any changes in ureteral caliber or peristalsis.

c. Bladder. Evidence which has been obtained during the past five years demonstrates that both the storage of urine in the bladder and its evacuation are mediated exclusively by the sacral parasympathetic nerves (Denny-Brown and Robertson, 1933; Evans, 1936; and Langworthy, 1940).* The sympathetic fibers regulate the flow of blood. They may also exert a slight influence on the internal sphincter. This has been maintained by Learmonth (1931), but denied by Denny-Brown and Robert-

* The sacral segments also give off the pudendal nerve to the external sphincter of the bladder. This has been regarded as a voluntary nerve, but the work of these investigators has shown that its tone is inhibited and that it opens only during the integrated act of micturition. It can only be closed voluntarily.

level, but the relation of the vagi to insulin secretion is in Long's opinion more questionable. Until more convincing facts are established, it would seem that the major control of carbohydrate metabolism is to be found in the activity of the anterior pituitary, adrenal cortex, and islands of Langerhans. It is still quite possible that their activity is regulated directly by the composition of the blood passing through them.

There is also a certain amount of evidence that protein metabolism is mediated by autonomic impulses from the diencephalon. Freund and Grafe (1912) showed experimentally that it is augmented by the sympathetic and inhibited by the parasympathetic nerves. The secretion of bile, on the other hand, is stimulated, though only partially, by the vagus (Eiger, 1915).* The observations of Bainbridge and Dale (1905) show that the musculature of the biliary system responds in general to vagus and splanchnic stimuli much as does the musculature of the gastrointestinal tract.

The action of the extrinsic nerves on the digestive secretions of the pancreas is still not thoroughly settled. Although the secretion of water, bicarbonate, and the digestive enzymes in the pancreatic juice is stimulated in part by the action of "secretin" in the circulating blood, the digestive activity of the pancreas is also controlled by its autonomic nerves. Beginning in 1878 Pavlov observed that atropine inhibited pancreatic secretion. More recent experiments by his students show that the vagus nerves excite the pancreatic acini to secrete digestive juice. Mellanby (1926) has carried out the most complete studies on pancreatic secretion and found that as a result of vagus stimulation the trypsin and amylase in the pancreatic juice are increased, whereas the liquid and bicarbonate content remain unchanged. (The secretion of the latter he ascribes to the action of "secretin.")

Neurogenic Control of the Urinary Tract.

a. Kidney. Transplantation of the kidney, successfully performed by Carrel and Guthrie (1906) proved that the totally denervated kidney can carry on all functions which are essential to life. The earlier studies on renal denervation, notably those of Quinby (1916) and Marshall and Kolls (1919), indicated a

temporary increase in urinary secretion. Nearly all investigators have agreed that denervation causes no change in the elimination of phenolsulphonephthalein, sodium chloride, lactose, urea, and many other substances. The most recent and carefully controlled experiments of Rhoads, Van Slyke, Hiller, and Alving (1934) on dogs showed no consistent effect on either the excretory efficiency of the kidney or on the renal blood flow. These results in animals have been confirmed in man by Page and Heuer (1935*A* and *B*). Measurements of urea clearance and volume of urine secreted from the normal and the denervated kidney (resection of nerve fibers in the renal pedicle) failed to show any significant difference over a period of months following operation.

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son (1933). Resection of the superior hypogastric plexus produces no alteration in the cystometrogram (see p. 376, Chap. XV).

Neurogenic Control of the Sex Organs. While the development and functional activity of the sex organs are largely under the control of the endocrine glands (anterior pituitary and adrenal cortex), their reflex adjustment to environmental changes is regulated by the autonomic system. In a general way the behavior of these opposed nerves follows the rules of homeostasis in other parts of the body. In states of well-being and contentment the parasympathetic holds the upper hand, and under these circumstances the pelvic viscera receive a maximal flow of blood and are easily stimulated. Under conditions of fear and worry the blood is shunted to the striated muscles and with it irritability of the genital tract and sexual desire are temporarily lost.

a. The Male Sex Organs. Kuntz (1919) has shown that in the testicle unmyelinated nerve fibers follow the distribution of the vessels and do not invade areas of secretory tissue or tubules except as they accompany the arteries and veins. This is presumptive evidence that the spermatic plexus governs spermatogenesis only by its control of blood flow to the testicle.

In the control of the complex processes that lead up to orgasm and ejaculation, the involuntary nerves play the double rôle of engorging the penis with blood and causing ejaculation by contracting the smooth muscle of the vasa deferentia, seminal vesicles, and prostate. Eckhard (1863) found that stimulation of the sacral nerves in the dog causes erection of the penis. When the nervi erigentes are cut, the vessels in the penis contract (Nikolsky, 1879). Langley and Anderson (1895) stimulated the lumbar sympathetic rami (second, third, and fourth) and demonstrated vasoconstriction of the penile vessels. These investigators also confirmed the previous observation of Budge (1858) that stimulation of the sympathetic nerves causes contraction of the entire musculature of the ducti deferentia and seminal vessels. In addition, it has been shown by Simeone (1933) that when these fibers are paralyzed viable spermatozoa no longer reach the seminal vesicles. Learmonth (1931) was able to show the discharge of seminal fluid in man on stimulation of the superior hypogastric plexus. After removal of the

plexus or injury to the first lumbar ganglia the power of ejaculation is lost,* although this operation does not impair the power of erection nor the sensation of orgasm. The results of these experiments clearly indicate the cause of sterility in the male after injury to the upper lumbar ganglia or superior hypogastric plexus.

b. The Female Sex Organs. In a general way the nervous control of the female genitalia is similar to that in the male. Kuntz (1934) has shown that, although the ovary is abundantly supplied with nerve fibers, their distribution is limited to the blood vessels and the fibromuscular tissue in the stroma. As in the male, sympathetic stimulation causes contraction of the smooth musculature of the tubular and glandular portions of the genital tract and constriction of the blood vessels. During sexual excitement the nervi erigentes cause engorgement of the clitoris and labia minora, a reaction comparable to erection in the male. This response is caused by a summation of psychic stimuli and afferent impulses conveyed from the external genitalia to the sacral cord by the pudendal nerve. At the moment of orgasm the reflex center in the lumbar cords emits an outburst of sympathetic stimuli, causing contractions of the Fallopian tubes, uterus, and Bartholin's glands.

Section of the extrinsic nerves to the female sex organs does not interfere with normal menstruation or reproduction. As far back as 1882 Rein reported birth of young in rabbits following section of all the extrinsic nerves to the uterus. Cannon et al. (1929) have observed normal parturition in their totally sympathectomized cats, and Fontaine and Herrmann (1932) have recorded cases of normal childbirth after resection of the superior hypogastric plexus. According to Gerstmann (1926) this can take place in women even after complete transection of the spinal cord.

In concluding this chapter on the nervous control of homeostasis one should pause to consider to what extent the autonomic system functions in an independent manner. The concept of its purely automatic activity, although long since disproved, tends to recur in current articles and in our thoughts. Even Langley

* We are obtaining increasing clinical evidence that males may not be sterile or have any alteration of sexual function after bilateral excision of the first or even the upper three lumbar ganglia.

(1921), who proposed the term "autonomic" in 1898, felt that it suggested "a much greater degree of independence of the central nervous system than in fact exists." In the twenty years since his book was written, a mass of evidence has accumulated which brings out a constant coördination of visceral and somatic activity. In the central nervous system it is not always possible to separate autonomic from cerebrospinal pathways. In the cortex, as shown in the beginning of this chapter, recent evidence has brought out a certain degree of autonomic representation, which is mainly localized in the motor and premotor areas. In the cerebellum, always considered the sole domain of somatic function, Moruzzi (1940) and Connor (1941) have discovered evidence for autonomic control over the medullary centers of respiration and circulation by the paleo-cerebellar cortex. On the other hand, representation of somatic activity in such a purely autonomic area as the hypothalamus has recently been pointed out by Hinsey (1940). Sheehan (1941) has summarized the interrelationship of the cerebrospinal and the vegetative systems by the statement that "one is left with a concept of a single nervous system physiologically speaking, where visceral and somatic activities are closely integrated, and where each is probably under a certain control of the other."

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Chapter V

PHYSIOLOGICAL ACTION OF DRUGS AND HORMONES

I. Pharmacology of the Sympathomimetic and Parasympathomimetic Compounds.

An understanding of the action of certain drugs and hormones is essential for a basic understanding of autonomic neurophysiology. Besides their rôle as chemical mediators in the transmission of nerve impulses and in propagating the autonomic discharge to denervated structures, these compounds are of great value in physiological investigation. The following is a classification of the neuro-hormones which are elaborated in the body and the most potent drugs which are used in the clinic and laboratory:

	Acting on the Sympathetic	Acting on the Parasympathetic
Stimulating	Epinephrine or adrenaline * Sympathin Ephedrine Amphetamine sulfate (Benzedrine)	Acetylcholine Pilocarpine
Depressing	Ergotoxine Nicotine	Atropine Nicotine

Much valuable information concerning the action of the autonomic nervous system has been gained by studying the reaction of laboratory animals to these substances, but unfortu-

* These compounds, when their formulae are known, should be [illegible] with [illegible] names, [illegible] thout a [illegible], whose [illegible] When [illegible] cifically [illegible]

nately their use in the clinic is limited. The factors which vitiate the therapeutic value of these preparations are the very limited duration of their activity, the difficulty of administration of some of the most active preparations (intravenous or intraventricular injection), and the fact that nearly all of them act with great intensity on the entire craniosacral or thoracolumbar divisions. For the sake of securing one desired result, many disagreeable or even dangerous effects are unavoidably produced. For this reason no attempt will be made to discuss all the properties of these substances nor their medical application in such conditions as bronchial asthma, somnolent states, migraine, and myasthenia gravis, where the autonomic nervous system is not directly concerned. The rather rare conditions which can be treated specifically by these substances are taken up in Part II, the discussion here being limited to the behavior of these compounds in so far as it is of value in understanding the physiology of the autonomic system and certain peculiar responses of smooth muscle and glands after denervation. For a more orthodox pharmacological description the reader is referred to Clark (1938) and a number of selected articles which are referred to in the following paragraphs.

Sympathetic Excitor Drugs

a. Adrenaline. The medulla of the suprarenal gland is formed embryologically from cells migrating out from the growing splanchnic nerves The secreting chromaffin cells are innervated directly by preganglionic neurons and are analogous to the cells of postganglionic neurons. They secrete a sympathomimetic hormone into the blood stream. Its active principle, $C_6H_3(OH)_2$—CHOH—CH_2—$NHCH_3$, was first isolated by Abel and called "epinephrine." It has come to be more widely known to the medical profession as "adrenaline" or by its trade name "adrenalin," and as "adrenine" to the physiologists when they refer to the actual secretion during life. The effects of adrenaline are practically identical with a widespread discharge of the thoracolumbar nerves, with the notable exception that the sweat glands are not stimulated.

From a therapeutic point of view the bronchodilator effect of adrenaline is of incalculable value to sufferers from bronchial asthma. Fortunately it is capable of relaxing bronchial spasm in such extremely small concentrations that it can be given safely by injection. This is also true of its hemostatic action when used in conjunction with procaine in local infiltration of the tissues. Under these conditions there is no pupillary dilator response and but little inhibition of the gastro-

intestinal tract. In the average individual there is but a slight rise in blood pressure and little acceleration of the heart. In order to obtain the latter effects in a constant degree, adrenaline must be given intravenously. Following intravenous injection it is used up rapidly in the tissues; its effects are therefore too short-lived to be of any general therapeutic value.

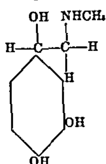
The point at which adrenaline produces its characteristic effect has never been exactly determined. It cannot act directly on the sympathetic nerves because its action persists, or is even increased, when the nerves have totally degenerated (see p. 116). Neither can adrenaline act directly on the contractile mechanism in the smooth muscle cells, because as Dale (1906 and 1913) has shown, when ergotoxine is administered these cells, although they retain their intrinsic contractile power, are no longer affected by it. These observations have narrowed the point of action of adrenaline down to some intermediate substance between the nerve endings and the contractile mechanism in the muscle cells Cannon and Rosenblueth (1937) have conveniently referred to this as the neuro-effector mechanism and have written a valuable monograph on the subject.

A final point of interest in the pharmacology of adrenaline is the reversal of its effects when given in minute amounts Langley (1921) has shown that relatively large doses contract the erector pilae muscles, a lesser amount contracts the tunica dartos, and small amounts contract the cutaneous arterioles. In contrast, still smaller doses under certain circumstances produce vasodilatation. This is due to the fact that adrenaline affects not only the vasoconstrictor mechanism, but also the vasodilator. As a general rule, however, the constrictor nerves are the more powerful. This constrictor preponderance can be unmasked by the use of ergotoxine, which paralyzes the vasoconstrictor response while leaving the dilator unaffected. As a consequence the injection of adrenaline after ergotoxine produces a fall in blood pressure.

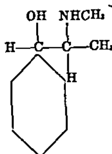
b. Sympathin. This little known, but physiologically most interesting substance is elaborated at the junctions of the sympathetic nerves with the smooth muscle cells. It was discovered by Cannon and Uridil (1921). Sympathin acts as a sympathetic activating hormone like adrenaline, but differs from the secretion of the adrenal medulla in elevating blood pressure even after ergotoxine, whereas adrenaline under these conditions causes a fall. It further differs by containing separate excitor and inhibitor fractions. The two forms of [illegible] adrenaline have been described [illegible] Up to date its formula is unknown and it has not been isolated outside the body.

c. Other Sympathetic Drugs. The alkaloid ephedrine, obtained from Ma Huang, and the synthetic compound amphetamine sulphate, or benzedrine, are related to adrenaline both chemically and pharmaco-

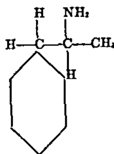
logically. Their similarity is shown in the structural formulae of the three compounds:



ADRENALINE



EPHEDRINE



AMPHETAMINE (BENZEDRINE)

Ephedrine differs from adrenaline clinically in being active when taken by mouth and in its more prolonged effect.

Benzedrine (amphetamine sulphate) resembles ephedrine in its effectiveness on oral administration and its prolonged action on the blood pressure (Myerson, Loman, and Dameshek, 1936; Michelsen, Adams, and Shinners, personal communication), but its most important property is a central stimulating action. This may be due to an ability to increase metabolism in the hypothalamic region of the brain, as has been suggested by Serota (1939). The drug is of value in the treatment of narcolepsy (Prinzmetal and Bloomberg, 1935), postencephalitic parkinsonism (Solomon and Prinzmetal, 1936), and certain depressive mental states (Myerson, 1936), and for reducing the depth of anesthesia and narcosis (Myerson, Loman, Rinkel, and Lesses, 1939; Michelsen and Verlot, 1939).

Sympathetic Inhibitor Drugs

a. Ergotoxine. Dale (1906), who described the pharmacological action of ergotoxine, demonstrated that it paralyzes the excitor action of sympathetic nerves, while leaving inhibitory sympathetic and all [illegible] of relaxing vasoconstrictor tone in the cutaneous vessels, it is unfortunately not a safe preparation. Such a drug, were it not too toxic for clinical use, would be of incalculable value in the therapy of Raynaud's disease.

b. Nicotine. The alkaloid of the tobacco plant in small doses stimulates and in larger amounts paralyzes synaptic junctions in the autonomic ganglia. Langley and Dickinson (1890), after painting the ganglia with nicotine, found that stimulation of the white communicant rami no longer resulted in cutaneous vasoconstriction or acceleration

of the heart, although stimulation of the gray rami still produced a characteristic response. From this observation Langley proved that the endings of preganglionic neurons in the white communicant rami form synapses in the peripheral ganglia with a second order of nerve cells, which in turn send non-medullated fibers into the gray rami.

Parasympathetic Excitor Drugs

a. Acetylcholine and Pilocarpine. These two drugs, which are not related chemically, have a similar stimulant effect on cells which are under the control of the parasympathetic nerves. Acetylcholine, which is produced at the endings of the craniosacral nerves, is destroyed in the body with extreme rapidity by a cholinesterase. For therapeutic use it must therefore be administered in the more stable form of acetyl β-methyl choline hydrochloride (mecholyl) or be protected from esterification by physostigmine (eserine) or prostigmine. As a result of physiological doses of these substances, the sudatory, salivary, and lachrymal glands, as well as the mucous glands of the respiratory passages and the glandular structures throughout the gastrointestinal tract, are roused to intense activity. There is a corresponding increase of muscle tone in both ends of the gastrointestinal tract. Myerson, Rinkel, and Dameshek (1936), who have studied the effect of mecholyl on the gastric juice, report that it stimulates the production of mucin and at the same time inhibits the secretion of pepsinogen and hydrochloric acid, thus producing a copious flow of alkaline gastric juice. The value of these drugs in paralytic conditions of the intestinal tract is discussed in Chapter XIV.

While these compounds, especially acetylcholine, give a striking vasodilatation of the vessels in the skin, they are unfortunately of little value in the treatment of Raynaud's disease. If given in really effective doses the patient suffers from drenching perspiration, salivation, gastrointestinal disturbances, and a fall in blood pressure. With smaller dosage, vasodilatation is negligible (Hunt and Taveau, 1906; Dale, 1914). An ingenious method for promoting the absorption of acetylcholine through the skin and thus producing local vasodilatation without systemic effects has been described by Duryee and Wright (1937). In this procedure, known as "iontophoresis," a galvanic current of 20 milliamperes is used to carry the drug through the skin. It has a limited value in the treatment of peripheral vascular disease.

b. Pilocarpine, Pituitrin, and Acetylcholine (Intraventricular Injection). The intramuscular or intravenous injection of posterior pituitary extract causes prompt blanching of the skin and mucous membranes and evacuation due to stimulation of the lower bowel. These responses are not due to any effect on the involuntary nerves, but to the direct action of pituitrin on smooth muscle. Cushing (1931) has produced the direct antithesis of this reaction by injecting pituitrin or pilocarpine into the cerebral ventricles. Under these circumstances there is an astonishingly prompt response characterized by flushing, profuse per-

spiration, salivation with retching and vomiting, and a marked fall in the body temperature—a generalized parasympathetic discharge. This reaction is abolished by atropine, which paralyzes the parasympathetic nerves, and by tumors which infiltrate the walls of the third ventricle and destroy the diencephalic nuclei. Cushing therefore reasoned that this effect was brought about by diffusion of the drug and direct stimulation of the autonomic nuclei which lie in the walls of the third ventricle.* In addition he drew the conclusion that the active principle of the neurohypophysis reaches the autonomic nuclei in part by diffusion through the cerebrospinal fluid and in part through the blood. This theory is in line with the work of Popa and Fielding (1930) and with Basir's observation (1932) that a form of "portal circulation" exists between the pituitary body and the hypothalamic centers, notably those in the tuber cinereum, but the presence of such a vascular link has been discredited by Wislocki (1938).

Cushing's hypothesis that secretion of the pars nervosa into the third ventricle influences the parasympathetic centers in the hypothalamus is opposed by many other considerations. Subsequent experiments on animals, including monkeys, have given far less definite reactions. Furthermore, there is no evidence that the parasympathetic system ever reacts with a diffuse discharge to natural stimuli, and the massive doses of drugs injected by Cushing were out of all proportion to normal concentrations. Rioch (1938) in discussing the studies on the presence of the active principle of the pars nervosa in the ventricular fluid stated that "it is clear that in the hands of the more careful workers the amounts found have been either nil or, in the words of Trendelenburg, 'ausserordentlich wenig.'" As has been pointed out by Resnick et al. (1936), the action may be entirely non-specific and due to potassium, oxalate, citrate, or phosphate ions. Rioch (1938) concluded that "it seems most likely that the results reported were due to non-specific (possibly vasoconstrictor) effects at the region of the floor of the fourth ventricle, affecting chiefly the vagal and depressor mechanisms."

Parasympathetic Inhibitor Drugs

a. Atropine. Atropine paralyzes the parasympathetic nerves. It inhibits the secretion of the salivary, gastric, pancreatic, and mucous glands, dilates the pupil, and prevents slowing of the heart when the vagus nerve is stimulated. Atropine also paralyzes the sweat glands. Inasmuch as the latter structures are innervated by the sympathetic nerves, this action of atropine was formerly difficult to explain. The paradox has been cleared up by the work of Dale and Feldberg (1934), who showed that the sympathetic postganglionic fibers to the sweat

* Henderson and Wilson (1936) have more recently found that a similar reaction occurs on the [illegible] amounts wh[illegible] They have sho[illegible] abolished by [illegible] been proved that these manifestations are due to specific action of the autonomic nuclei in the diencephalon.

glands are cholinergic, in contrast to their usual adrenergic properties (see below).

b. Nicotine. The action of nicotine on the parasympathetic system is similar to its effect on the sympathetic described above. It blocks synapses between the central and peripheral motor neurons which lie in the visceral plexuses.

II. Chemical Mediators of Autonomic Nerve Impulses

Adrenaline, Sympathin, and Acetylcholine. Chemical mediation of nerve impulses was first suggested by the pioneer work of Elliott (1905) on medulli-adrenal secretion. As Cannon (1931) has put it, "any general stimulation of the sympathetic division of the autonomic nervous system causes a secretion of adrenine, and this adrenine, widely distributed by the blood, has as a rule the same effect as the sympathetic impulses." In addition to this chemical substance which is secreted into the blood from a single pair of ductless glands, more recent studies have shown that similar substances are set free by the autonomic nerve impulses near or within all the cells which they supply. Otto Loewi (1921) first called attention to this by showing that the fluid perfused through the heart of a frog during vagus stimulation contained a substance capable of slowing the heart of a second frog. Gibbs and Szelöczy (1932) have extracted a similar compound from the submaxillary glands of mammals by stimulating the chorda tympani nerve. This work has been confirmed and enlarged by numerous other investigators, notably by Dale (1933, 1934). The parasympathetic substance appears to be a very active ester of choline and probably acetylcholine itself. It has also been established that a neuro-hormone, which pharmacologically resembles acetylcholine, is secreted at the ganglionic synapses (Feldberg and Gaddum, 1934; Feldberg and Vartiainen, 1934) and also at the endings of the preganglionic splanchnic fibers on the adrenaline secreting cells in the adrenal medulla (Feldberg, Minz, and Tsudzimura, 1934).

A corresponding substance which is elaborated at the endings of the sympathetic nerves was discovered by Cannon and Uridil (1921) and later called *sympathin*. When the splanchnic nerves to the liver were stimulated in animals which were digesting meat, the denervated heart accelerated even after inactivation of the adrenal glands. Cannon thought of a substance liberated from the sympathetic endings in unstriated muscle, and with

Newton and Zwemer (1931) showed that the denervated heart is accelerated when the sympathetic nerves to the cat's tail are stimulated. According to Cannon and Bacq (1931) this new hormone, sympathin, comes from all smooth muscle, regardless of whether it is excited or inhibited by the thoracolumbar nerves. *Sympathin E*, the excitor form of this substance, is liberated from the type of unstriated muscle which contracts in response to sympathetic nerve stimulation (cutaneous blood vessels, erector pilae muscle, etc.). An inhibitor form, *sympathin I*, is set free in the smooth muscle of the intestine, which is inhibited by sympathetic stimuli (Cannon and Rosenblueth, 1933).

The physiological function of the vagus substance and of sympathin is to distribute the autonomic impulse through smooth muscle. Stöhr (1928) has reported that only one smooth muscle cell in a hundred receives a nerve ending. These chemical mediators render an individual nerve filament for each contractile element unnecessary. As Cannon and Rosenblueth (1937) state the case, "when the sympathetic system goes into vigorous action . . . it liberates sympathin at perhaps all its myriads of endings —sympathin in such excess that it overflows and enters the circulation; and it liberates, also into the circulation, adrenine. These two substances . . . have additive effects. To what degree sympathin may be important in the presence of a normal discharge of adrenine has not been determined, but it is clear that locally produced sympathin, circulating sympathin, and circulating adrenine all work together to unify and synchronize the operation of the sympathetic system. Even when an organ has been deprived of its sympathetic fibers the circulating agents will force it into coöperation with the other affected viscera." (See below.) Furthermore, it has been shown that both adrenine and sympathin are liberated by stimulation of the hypothalamus (Magoun, Ranson, and Hetherington, 1937). In contrast to the sympathomimetic hormones the vagus substance is rapidly destroyed, and therefore produces a very localized response. These effects are in line with the general behavior of the sympathetic and parasympathetic systems of nerves.

The action of these neuro-hormones and their fundamental importance in the wide field of neurophysiology has been intensively investigated during the past few years. It now appears probable that a chemical step intervenes between the electrical

discharge which is transmitted along the nerve fiber to its ending and the effector in the contracting muscle or secreting gland cell. This theory has met with numerous objections, but overwhelming evidence in its favor has recently been presented by Cannon (1939*A*). In the case of craniosacral nerve endings on unstriated muscle and glandular structures, and also of somatic nerve endings on skeletal muscle, the reaction is carried out by the acetylcholine-like substance. This is broken down by cholinesterase in a few milli-seconds and so produces a very localized response.* The more generalized discharge from the thoracolumbar nerves is mediated by sympathin. This substance acts on local structures with greatest intensity, but being less rapidly destroyed it ultimately spills over into the circulating blood and is thereby widely distributed to smooth muscle and glands throughout the body.

It has been pointed out above that there are certain peculiarities in the chemical mediation of the sympathetic nerve impulse, notably in the ganglionic synapses, adrenal medulla, and sweat glands, where the mediator has been found to be acetylcholine. Dale (1934) has conveniently classified autonomic neuro-effector mechanisms into adrenergic and cholinergic fractions (Fig. 24). Those who would pursue this interesting subject further should refer to Dale's paper and the monograph by Cannon and Rosenblueth (1937).

Sensitization of Denervated Structures to Chemical Mediators. It has been emphasized by Cannon (1933) that the point of action of the chemical mediators of autonomic impulses lies between the nerve endings and the responsive mechanism in the smooth muscle cells. The exact way in which the neuro-effector mechanism is altered has not been determined, but its sensitiveness does not disappear when the nerve itself degenerates. On the contrary, it is greatly increased. As a result, the injection of these substances produces an exaggerated response after destruction of the autonomic nerves.† This interesting phenomenon was

* The acetylcholine-like parasympathomimetic hormone is unstable because it is rapidly broken down by cholinesterase into less active choline. This action is largely prevented by eserine (physostigmine) and the closely related compound, prostigmine. The action of sympathin can likewise be reenforced by

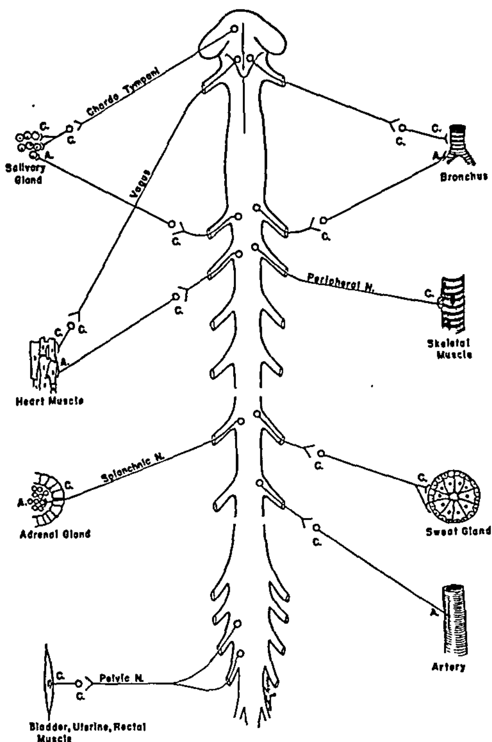


Fig. 24. Adrenergic and cholinergic nerve endings.

A. Adrenergic nerve ending.
C. Cholinergic nerve ending.

(Redrawn and modified from Dale, 1934)

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(1936) report that the pupillary sphincter, sensitized by section of the ciliary nerves, contracts to doses of acetylcholine which are without effect on the normal muscle. The same is true of the superior cervical ganglion whose cells, innervated by the preganglionic fibers, respond with increased effect to acetylcholine after chronic denervation (Cannon and Rosenblueth, 1936). List and Peet (1938) have likewise shown that the sweat glands become increasingly sensitive to acetylcholine (and to pilocarpine) after sympathectomy. The same is true of skeletal muscle (Bender, 1938). These phenomena have been stated by Cannon (1939*B*) as a general law of denervation: "When in a series of efferent neurons a unit is destroyed, an increased irritability to chemical agents develops in the isolated structure or structures, the effect being maximal in the part directly denervated."

The Clinical Importance of the Sensitization Phenomenon. Robert Edes (1869), an extraordinarily astute observer who wrote a physiological treatise on the sympathetic nervous system seventy years ago, deserves the credit for having first noticed that the vessels in the denervated ear of a rabbit soon begin to constrict with excitement: "If the animal is loose, so that there is difficulty in catching it for examination, or it is excited by being handled, the normal ear often equals, or, as I have seen some days after the operation, surpasses in temperature the opposite side."

Sensitization of the neuro-effector mechanism on the smooth muscle cell to internal secretion, which can still reach it through the blood stream after denervation, has a direct surgical application of great importance. The Meltzers (1903*A* and *B*) observed that the arteries in the rabbit's ear after sympathectomy are intensely constricted by subcutaneous injections of adrenaline and remain so for hours, while the normal ear shows a distinct vasodilator response. This phenomenon could not be explained at the time, although the reason now is obvious. Smithwick, Freeman, and White (1934), while investigating the failure of sympathectomy to relieve vasospasm in certain cases of Raynaud's disease, found that physiological dilutions of adrenaline were capable of producing intense vasoconstriction in the denervated arteries. This response in human arteries is exactly similar to the phenomenon the Meltzers observed in rabbits. Freeman, Smith-

first pointed out by T. R. Elliott (1905) in the action of adrenaline. Cannon, Lewis, and Britton (1926) could not produce a heart incapable of acceleration after total denervation until they had sectioned the splanchnic fibers to the adrenal glands and the nerve supply to the liver, which can also elaborate sympathin (from the nerve endings on its blood vessel walls) into the circulating blood. Meltzer and Auer (1904), and long before them Budge (1855), Schiff (1868), and Edes (1869) had shown that when the iris is deprived of its sympathetic innervation it not only continues to dilate after injection of adrenaline, but dilates after an amount so minute that the normally innervated iris remains completely unaffected. Hartman, McCordock, and Loder (1923) have demonstrated the sensitivity of the denervated iris to cold, pain, and fear; also the abolition of this effect after resection of the adrenal glands.

A more thorough analysis of this basically important phenomenon has been made by Hampel (1935). By observing the quantitative responses of the nictitating membrane on successive days after denervation, he has demonstrated that the response reaches its maximum in about eight days, and that postganglionic denervation brings about an increase in sensitization of the neuro-effector mechanism which is nearly twice as great as after preganglionic denervation. The work of Simeone, Cannon, and Rosenblueth (1938) and Simeone (1938) has shown that incomplete denervation of any structure which is under the control of the autonomic nervous system results in little functional impairment. This is due to diffusion of chemical mediators from the cells which retain their nerve supply to those which are denervated, but have become sensitized thereby. This means that *surgical denervation must be complete, or it will be of little value.* Furthermore, *the sensitization phenomenon accounts for the fact that there is no chronic flaccid paralysis of smooth muscle.* While adrenaline characteristically stimulates denervated smooth muscle, it is of interest to find that structures like the intestinal and uterine musculature, which are inhibited by the sympathetic nerve impulse, become sensitized to the inhibitory action of adrenaline (Luco, 1937; Youmans and Meek, 1938).

In addition to these changes which follow denervation in adrenergic neuro-effector mechanisms, similar phenomena have been observed in the cholinergic structures. Shen and Cannon

skin temperature which occurs under similar conditions in denervated fingers in Raynaud's disease three months after cervicothoracic ganglionectomy. With such a dilute solution of adrenaline there is no vasoconstrictor response in the normal extremity.* Vasoconstriction is also absent in the finger when its nerves have been only temporarily paralyzed with procaine. That the human adrenal is capable of secreting sufficient medullary hormone to produce this response is demonstrated in Figure 26, a record of adrenal secretion stimulated by insulin hypoglycemia. This vasoconstrictor response to insulin hypoglycemia also occurs in the denervated ear of a rabbit, but is abolished after inactivation of the adrenal glands (by resection of the left adrenal and denervation of the right). We have found that this sensitization to adrenaline, which manifests itself on degeneration of the postganglionic neurons, lasts only as long as sympathetic paralysis remains complete; with evidence of the reestablishment of sympathetic tone the phenomenon disappears. This has been corroborated by Simeone (1937).

Grant and Bland (1932) were the first to make a thorough investigation of the residual vasoconstrictor responses in the ears of rabbits after peripheral denervation. White, Okelberry, and Whitelaw (1936) found that after postganglionic denervation the blood vessels in rabbits' ears maintain a complete vasomotor paralysis for barely forty-eight hours (Fig. 27A). After this initial period the arteries become extraordinarily sensitive to circulating adrenine and to sympathin as well. On the slightest cooling, muscular exertion, discomfort, or fear the arteries of the denervated ear become intensely constricted (Fig. 27B). After adrenal inactivation this response is greatly diminished (Fig. 27C). We have, however, observed a moderate degree of vasoconstrictor power in the denervated ear, even after inactivation of the adrenals, following intense stimulation of the sympathetic nervous system by cold and anesthesia. This is probably due to secretion of the second sympathetic hormone, sympathin. In contrast, when the preganglionic neurons are interrupted either by cutting the upper five anterior thoracic spinal roots or by resection of the inferior cervical sympathetic

* Fatherree and Allen (1938) have shown that if adrenaline is injected in unphysiologically large concentrations intra-arterially or intravenously, even the normal finger will exhibit a vasoconstrictor response.

wick, and White (1934) have also shown that the human adrenal can secrete a sufficient amount of adrenine in response to cold, emotion, and insulin hypoglycemia to account for some of the failures of sympathetic denervation. On testing the response of

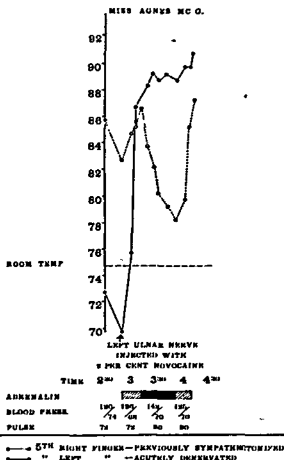


FIG 25 Vasoconstrictor effect of adrenaline on digital blood vessels after degeneration of postganglionic sympathetic rami

Contrast absence of constriction in the acutely denervated area. (From Freeman, Smithwick, and White, 1934, courtesy of *American Journal of Physiology*.)

a sympathectomized hand on the second, sixth, eighth, and eighteenth days after destruction of the upper thoracic ganglia by alcohol injection, it was found that during the first week the intravenous injection of a physiological solution of adrenaline (1 part in 250,000) produced only a slight fall in surface temperature. On the eighth day, however, there was a striking vasoconstrictor response. Figure 25 shows the characteristic fall in

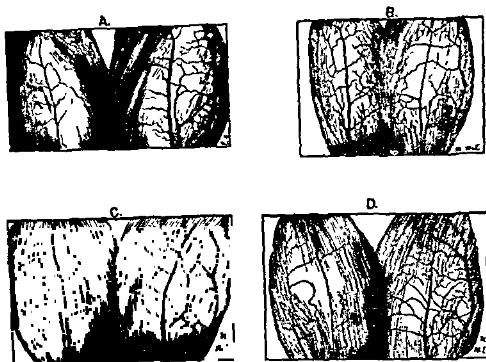


FIG. 27. Vasomotor reflexes in ears of rabbits.

In each figure the left is the normal control ear, in the right the sympathetic vasoconstrictor fibers have been interrupted by various methods.

A. Continuous maximum vasodilatation in denervated right ear of rabbit twenty-four hours after cutting postganglionic sympathetic neurons. Room temperature 56°

B Maximum vasoconstriction secondary to excitement in denervated right ear of rabbit eight days after destruction of postganglionic sympathetic neurons Room temperature 72°.

C. Persistent vasodilatation of right ear after section of postganglionic sympathetic neurons and subsequent inactivation of the adrenal glands. Room temperature 70°.

D Persistent vasodilatation of right ear after destruction of preganglionic sympathetic neurons on right side by sectioning the upper five thoracic spinal roots. Room temperature 70°. Complete vasodilatation persisted after animal had been subjected to a temperature of 40° for two hours, although the body temperature fell 5°.

ganglia, the arteries in the rabbit's ear remain dilated (Fig 27D). As the postganglionic neurons remain intact after this procedure, the ear vessels become only minimally sensitized to circulating hormones. In a further investigation White, Okelberry, and Whitelaw (1936) have compared the different degrees of sensitization which result from destruction of the preganglionic and postganglionic vasoconstrictor fibers to the hand of the monkey. These statistics are closely similar to those presented by Hampel (1935) for the nictitating membrane of the cat and by Grant (1935) for the rabbit's ear—i.e., after preganglionic sympathec-

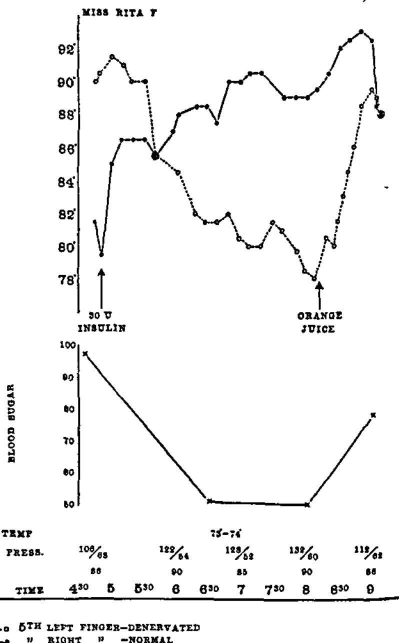
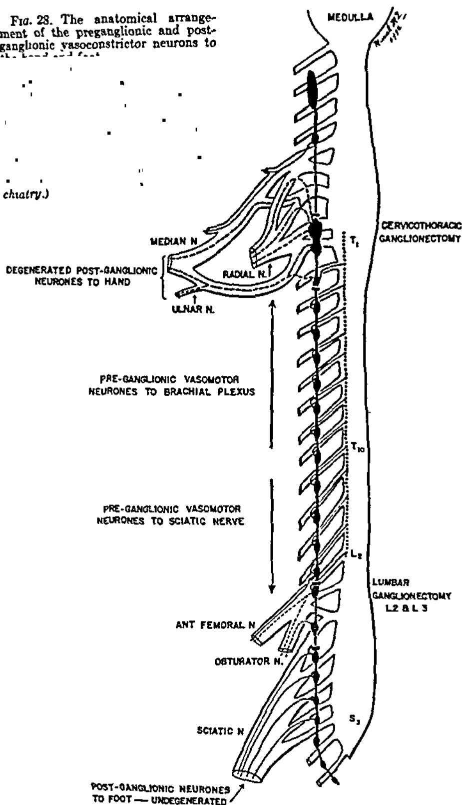


Fig. 26. Vasomotor responses in hands on insulin excitation of adrenal medullas

Vasoconstriction in hand after nerve degeneration and vasodilatation in normal extremity (From Freeman, Smithwick, and White, 1934, courtesy of *American Journal of Physiology*)

Fig. 28. The anatomical arrangement of the preganglionic and postganglionic vasoconstrictor neurons to

chiatry.)



tomy the response to circulating adrenaline and sympathin is less than half that found after degeneration of the postganglionic neurons.

This increased sensitization which occurs after postganglionic denervation is of fundamental clinical importance. It accounts in large part for the poor circulation which develops within a fortnight after injury to a major peripheral nerve (Atlas, 1938). In the first edition of this book it was suggested that this phenomenon explained the inferior results of cervicothoracic ganglionectomy in Raynaud's disease in the hand and the strikingly better results obtained after lumbar ganglionectomy for the same condition in the foot. Figure 28 shows that resection of the inferior cervical, first, and second thoracic ganglia destroys the great majority of cells which give rise to the postganglionic vasoconstrictor fibers to the arm, whereas removal of the second and third lumbar ganglia leaves intact these postganglionic neurons to the sciatic nerve which originate in the fourth lumbar and upper three sacral ganglia. That preganglionic sympathectomy results in more effective peripheral vasodilatation has since been corroborated by numerous workers, notably by Lewis (1938), by Simmons and Sheehan (1939), and by Foerster (1939). Ascroft (1937) has verified this assumption by showing that the obvious vasodilatation of the monkey's leg after lumbar sympathectomy disappears after subsequent resection of the sacral ganglia. The application of these important physiological principles to man are discussed in Part II.

In recapitulation, the outstanding implications of clinical importance to be derived from the pharmacological work which has been described can be condensed into a single sentence: *Paralysis after denervation of smooth muscle is very different from that seen in skeletal muscle, because there is no lasting flaccid paralysis.* Restoration of tone is due in part to the sensitization of the neuro-effector mechanism to circulating hormones. There is also some suggestive evidence that the peripheral sympathetic ganglia develop an independent activity after all their central connections have been cut (Govaerts, 1935).* Cannon (1937) feels in addition that the maintenance of tone must

* We have obtained clear-cut evidence that decentralized human ganglia emit a striking outburst of impulses for a short period after preganglionic denervation (see p. 175)

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Chapter VI

PHYSIOLOGY OF VISCERAL PAIN *

According to Langley "the autonomic nervous system consists of the nerve cells and nerve fibres by means of which efferent impulses pass to tissues other than multi-nuclear striated muscle." Thus by strict definition the parasympathetic and sympathetic nerves, which arise from the brain stem and the thoracolumbar and sacral portions of the spinal cord, are purely motor in function and control homeostasis. The fact that apparently all forms of visceral pain can be relieved by sympathectomy does not fit into this concept, but the paradox has been explained by recent findings of the neurophysiologists. Their investigations have shown that afferent nerve fibers, which differ in no way from those in a sensory nerve to the skin, run in the cardiac, splanchnic, and other sympathetic trunks. These axons differ from the classical autonomic fibers in having no synapses in the peripheral ganglia and in entering the spinal cord over its posterior roots (see Chap. III). The endings of the viscerosensory fibers are identical with those found in the skin and sclera. These are illustrated in Stöhr's monograph (1928). The Vater-Pacinian corpuscles that are found throughout the mesenteries have been studied by Sheehan (1932) and their degeneration observed after section of the splanchnic nerves. It therefore appears that viscerosensory and cutaneosensory fibers are identical both in histological characteristics and in electrical conduction. For the purpose of clarity, therefore, afferent axons from the internal organs will be referred to as the viscerosensory fibers, in contrast to the true autonomic or visceromotor fibers of Gaskell and Langley. Contrary to current opinion, Langley (1903) was well

* [illegible] by [illegible] *Its* [illegible] pp. [illegible]

aware of the afferent fibers to the viscera in the craniosacral and sympathetic pathways. He regarded these as belonging to the somatic system. He also realized that their number was relatively small and that therefore the threshold of visceral sensation was high. It is of interest in this respect to quote Langley's ideas on this important matter: "All that seems to me possible at present toward arranging afferent fibres into autonomic and somatic divisions is to consider as afferent autonomic fibres those which give rise to reflexes in autonomic tissues, and which are incapable of directly giving rise to sensation; and to consider all other afferent fibres as somatic . . . since the vagus, the pelvic nerve, and every white ramus of the sympathetic can give rise to pain."

A thorough understanding of the visceral sensory pathways is of the greatest practical importance to the neurosurgeon interested in the control of pain. The approach to this subject has been far from easy, not only because the objective study of pain by laboratory experiment is difficult, but also because of early theories which by very strength of tradition have stood in the way of progress. For these reasons the exposition of present concepts of pain in visceral diseases forms a most important chapter in this book.

The relative insensibility of the viscera is common knowledge. William Harvey (quoted by Goltz, 1863) tested cardiac sensation in the son of Count Montgomery, in the presence of King Charles I. The young man had suffered a severe injury a few years before which had opened his chest cavity widely and left the beating heart exposed. Harvey observed that touching the heart failed to arouse the slightest sensation. By animal experiments von Haller (1760) first established the insensibility of the visceral pericardium, pleura, and peritoneum to mechanical stimulation. After the advent of local anesthesia Lennander (1901) went so far as to state categorically that the viscera were wholly insensitive, and that only traction or irritation of the parietal peritoneum could arouse painful sensations.

Progress in the study of visceral pain followed the discovery of the "adequate stimulus." According to Sheehan (1936) the first conception of this idea is to be found in the writings of Whytt (1751), but it then passed into oblivion for another century and a half. The experiments of Hurst (1911), Schrager and

Ivy (1928), and Davis, Pollock, and Stone (1932) have demonstrated that distention of any hollow viscus is painful; Ryle (1926, 1928) amplified Hurst's conception by emphasizing contraction of smooth muscle in the hollow viscera as an adequate physiological stimulus. In addition the importance of the chemical products of exercising muscle in the presence of a deficient blood and oxygen supply has been ably set forth by Sutton and Lueth (1930) and by Moore (1938). Frequent operative reports have pointed out that pain results from crushing arteries (Leriche, 1927; Livingston, 1930), while Odermatt (1922) and Spiegel and Wassermann (1926) have produced pain by distending the larger arteries. Sudden distention or strong contraction of any part of the gastrointestinal or genitourinary tracts, rapid stretching of the capsule of such solid viscera as the liver and spleen, and abrupt anoxemia of the cardiac musculature are now recognized as the causes of pain in visceral disease.

Early theories avoided the possibility of direct pain transmission in three ways:

First, by assuming that violent contractions of the abdominal viscera must cause traction on the mesentery and therefore pull on the somatic nerves in the parietal peritoneum (Lennander, 1901).

Second, that some form of afferent impulse, but not true pain, travels up the splanchnic and other visceral nerves as far as the posterior horn of the spinal cord. There the bombardment of visceral impulses sets up an irritable focus * and diminishes the threshold for the somatic sensory impulses which are constantly entering the same segment of the cord from the periphery of the body. Normal subconscious impulses are thus magnified to actual pain. This is referred by the patient to cutaneous areas (Head zones) which share a common segmental spinal innervation with the diseased viscus (Fig. 29). It is of historical significance that Head (1893), who first made a careful study of the segmental levels to which visceral pain is referred, pointed

* This so-called "irritable focus" is not a satisfactory physiological concept. Mackenzie (1912) stated that "this stimulus [from the diseased organ] may be of the kind that affects neighboring nerve cells, and these nerve cells react according to their functions. When such stimulation affects a sensory nerve, pain arises, which is referred to the peripheral distribution of the nerve so stimulated." For a more satisfactory neurophysiological interpretation of the "irritable focus" see paper by Hinsey and Phillips (1940), which is summarized (p. 138).

out the interesting fact that "the sensory distribution of the sympathetic" corresponds with Edgeworth's (1892) chart of the sympathetic rami which carry large (sensory) axons and also "follows the lines laid down by Gaskell (1886) for the course of the motor and inhibitor fibres."

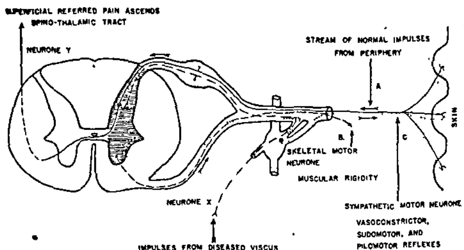


FIG 29 Diagram to illustrate Mackenzie's theory of referred pain.

Afferent impulses from a diseased viscus enter the posterior horn of the spinal gray matter over neuron X and set up the "irritable focus" (shaded area). The normally subconscious afferent impulses from the body surface which traverse neuron A now jump the synapse to neuron Y and reach the thalamus as pain which is referred to characteristic cutaneous areas The motor neurons B and C may also be discharged and cause reflex rigidity of skeletal muscle, or vasomotor, sudomotor, and pilomotor phenomena

This viscerocutaneous theory of Mackenzie (1893 and 1923) has been made to account for all forms of visceral pain. Although this cannot be accepted today, the theory explains in a satisfactory manner why hyperalgesia of the skin, accompanied at times by sweating and goose-flesh, reflex rigidity of the muscles, and frequently intense superficial pain, may be experienced by the patient in areas distant from the underlying inflamed organ (e.g., the pain in the right scapular region which is so often felt in gall bladder disease, the inguinal and testicular pain of renal colic, and the pain which radiates down the arm in angina pectoris). The demonstration by Weiss and Davis (1928) that simple procainization of the skin in the areas of referred pain is sufficient to cause its relief, affords confirmation of the presence of some form of viscerocutaneous reflex. However, as these authors point out, a dull, deep form of pain may persist after

complete cutaneous anesthesia. This is usually felt in the region of the diseased viscus itself and cannot be explained on the basis of Mackenzie's theory. Boyden and Rigler (1934) have likewise noted the persistence of deep pain under an anesthetized area when the interior of the duodenum is stimulated with a faradic current. Recent evidence which necessitates a modification of this theory is given below.

Morley (1931) in his book on abdominal pain points out numerous objections to Mackenzie's conception of the viscerocutaneous mechanism of referred pain. Morley states that pain from the internal organs is never accurately localized on the surface of the body nor accompanied by deep tenderness or reflex rigidity of muscle until the disease process has spread to the parietal peritoneum. Instead of a viscerocutaneous spread of referred pain he would substitute the idea of a peritoneocutaneous mechanism. He believes that well localized superficial pain arises only from irritation of nerves which are sensitive to those stimuli that produce pain when applied to the surface of the body. As evidence for this he points out that when pain is referred to a clearly defined point from a gastric ulcer, inflamed gall bladder, or acute appendix, the inflammatory process has always spread to the parietal peritoneum. This concept is a distinct aid in the explanation of referred pain in certain diseases of the peritoneal and pleural cavities, but it is not as satisfactory as Mackenzie's theory in accounting for such forms of referred pain as are seen in angina pectoris, where there is no inflammatory process and no possible contact of the heart with the intercostal nerves.

A *third* possible mechanism of visceral pain has been described by Davis and Pollock (1932). As a result of observations made by Langley (1921) and by Ranson and Billingsley (1918) it is comomnly supposed that there are no sensory fibers traversing the superior cervical sympathetic ganglion,* yet stimulation of this structure is often painful. This pain is relieved only by section of the trigeminal and the upper cervical posterior roots. Davis and Pollock therefore concluded that stimulation of this ganglion produces pain through sympathetic motor impulses to

* Heinbecker (1932) has observed large myelinated fibers with the characteristic conduction rate of afferent sensory axons in the upper portion of the cervical sympathetic trunk, but believes that they enter the vagus.

the skin and blood vessels of the face. They did not venture to give an exact reason why motor stimulation of structures containing smooth muscle should be painful, beyond hazarding the guess that it might be due to the liberation of a metabolite which in turn stimulates the ordinary sensory endings of the somatic nerves. Pollock and Davis (1935) believe that a similar sympathetic mechanism plays a rôle in the reference of pain to the shoulder tip when the phrenic nerve is stimulated. Penfield (1925) has attempted to explain the pain of angina pectoris on a similar basis, assuming that afferent stimuli from the heart set up painful disturbances in the skin of the precordium and arm by means of sympathetic axon reflexes. This theory of the production of pain by the liberation of a painful substance in the skin has never been confirmed. Indeed a recent article of Hinsey and Phillips (1940) casts considerable doubt upon its validity, as in an experience of Livingston which they report pain from stimulating the diaphragm was felt in an area of skin which had been fully anesthetized with procaine.

Although it is agreed that the theory of referred pain explains an important (and possibly the most acute) part of the sensation in visceral disease, and even granting that axon reflexes may cause reflex constriction of the cutaneous blood vessels which at times may be painful, both mechanisms fall short of explaining the entire picture seen in severe visceral pain. Besides the superficial referred pain, there is frequently a deep-seated distress which may be localized by the patient close to the diseased organ. This situation was clearly recognized by James Ross (1887) and Henry Head (1893). Although the names of both men are commonly associated with that of Mackenzie, each of them believed that in addition to the referred "somatic" pain a deep, heavy "splanchnic" pain was felt in the region of the diseased organ. In Ross' words:

> Disease of an internal organ—say the stomach—is accompanied by pain over the seat of the organ—the epigastrium in the case of the stomach—a pain that may be regarded as of splanchnic origin and named accordingly the splanchnic pain In addition to this pain, the patient complains of pain between the shoulders and in front of the chest . . . The splanchnic nerves of the stomach are derived from the fourth and fifth, and probably the sixth dorsal nerves, and when the splanchnic peripheral terminations of these nerves are irritated the irritation is conducted to the posterior roots of the nerves, and

on reaching the grey matter of the posterior horns it diffuses to the roots of the corresponding somatic nerves and thus causes an associated pain in the territory of distribution of these nerves, which may appropriately be named the somatic pain.

It was Ross who first suggested the idea of an "irritable focus" in the cord, but Mackenzie, in incorporating this valuable concept into his theory, disowned the idea of direct visceral sensation. In essential agreement with Ross, Head explains the known facts so well that his words deserve to be quoted at length:

> Thus, as our viscera are so notoriously insensitive, and as we have never had the opportunity of developing the sense of localisation in them, owing to their inaccessibility to touch, it is not to be wondered at that the maximum pain is not felt in the organ affected . . . A painful stimulus to an internal organ is conducted to that segment of the cord from which its sensory nerves are given off. There it comes into close connection with the fibres for painful sensation from the surface of the body which also arose from the same segment. But the sensory and localising power of the surface of the body is enormously in excess of that of the viscera, and thus by what might be called a psychical error of judgment the diffusion area is accepted by consciousness, and the pain referred on to the surface of the body instead of on to the organ actually affected. I do not mean to state that pain is never referred to the organ affected. Far from it. The pain is frequently felt in the organ itself, but it is "dull," "heavy," "wearing," and not "sharp," "aching," "stabbing," like the referred pain.

Important modifications in our concepts of the viscerosensory mechanism have taken place in the last few years. In his interesting monograph on abdominal pain, Morley (1931) has gone back to Ross' original concept of a dual *transmission* of pain from the internal organs, both direct and referred. Experiments on animals, as well as increasing clinical experience, are showing that visceral pain is not entirely referred to the cutaneous pathways and that direct transmission is of primary importance. Experiments have been reported by Lewis and Kellgren (1939) which brings out the fundamental similarity in the conduction of painful stimuli from all the deeper portions of the body, regardless of whether they originate in a viscus, or in the ligamentous structures, or in the deeper layers of skeletal muscle. By stimulating an upper thoracic interspinous ligament or the belly of the rectus abdominis muscle these investigators found

it possible to provoke pains with accompanying subjective sensations and visceromotor reflexes that are indistinguishable in quality from, as well as similar in distribution to, those of angina pectoris or abdominal colic. From these observations they have drawn the conclusion that "there is no special form of pain, referred or otherwise, and no special viscerosensory or visceromotor reflex, which is the hallmark of visceral disease." In addition Lewis and Kellgren point out that deep somatic and visceral structures are supplied by a common set of afferent nerves (including pain fibers) and that this common system is responsible for all the pain and referred phenomena of visceral disease.

The explanation of referred pain on the basis of Mackenzie's concept of an "irritable focus" has always been difficult to comprehend on account of its vagueness. But the theory of referred pain and the mechanism of visceromotor and somatomotor reflexes take on real meaning if we adopt the ideas of Hinsey and Phillips (1940) and "assume that both somatic and visceral afferent fibers carry impulses which affect a common pool of secondary neurons, and that the principles of summation and inhibition are applicable." They agree that visceral afferent impulses may inhibit or facilitate muscular reflexes or change the threshold in the spinal cord to afferent painful impulses from the periphery by virtue of their terminating upon the same group of neurons. But in addition they have found that viscerocutaneous reflexes are not essential for the sensation of pain, which may be felt in the midst of a completely anesthetized area of skin. In animals evidence of pain is still clearly evoked by distention of the gall bladder (Davis, Pollock, and Stone, 1932) or by ischemia of the myocardium (White, Garrey, and Atkins, 1933) after desensitizing the thoracic wall by cutting the intercostal nerves peripheral to the point of origin of the sympathetic rami communicantes, although it is abolished by cutting the splanchnic or cardiac nerves, or by cutting the corresponding thoracic posterior spinal roots. An example of the failure of cutaneous desensitization to relieve coronary pain in man is recorded on page 286. Here the characteristic anginal attacks over the precordium and arm were relieved by cervicothoracic ganglionectomy, but pain referred to the left side of the occiput and neck was not influenced in any way by cutting the great

occipital nerve and other branches of the superficial cervical plexus.

Further light on the conduction of visceral pain has been derived from direct stimulation or destruction of the sympathetic trunks in man. For example, Bentley and Smithwick (1940) carried out a series of experiments in this hospital on patients before and after bilateral resection of the splanchnic nerves and the lower thoracic and first lumbar ganglia for essential hypertension. Epigastric pain produced by insufflation of a balloon in the duodenum to a certain pressure disappeared to the right of the midline after a right-sided operation and the same degree of distention was no longer felt after bilateral denervation. Adson (1935) and Leriche (1937) have stimulated the splanchnic nerves in the course of operations under spinal anesthesia. In Adson's case stimulation of the major splanchnic nerve produced pain near the upper part of the scapula, whereas the pain from the minor splanchnic was referred to the lower angle of the scapula. When the celiac ganglion was stimulated, the patient noted pain in the shoulder, but when the peripheral fibers of the ganglion were pinched he described an aching sensation in the lower abdomen. Leriche and Fontaine (1929) have also stimulated the stellate ganglion in the course of operation on patients with angina pectoris. The patients invariably complained of a sense of oppression deep down in the chest around the region of the heart. Additional data on the direct investigation of visceral sensation in man have been reported by Learmonth (1931), who records that a patient under low spinal anesthesia referred pain quite accurately to his bladder when the superior hypogastric plexus was crushed in the course of a presacral neurectomy.

In recapitulation of this discussion of visceral pain and the theories of its conduction, we would call attention again to the presence of axons in the visceral nerves identical in appearance and in electrical conduction to somatic sensory fibers. This anatomical finding is supplemented by physiological evidence and points conclusively to the basic similarity of visceral sensation and that which arises in deep somatic structures. Only through practice do the cutaneous nerves become endowed with the property of accurate localization. This sense is undeveloped in the new-born infant. It is not reasonable that it should ever

develop to any degree of accuracy in the deeper structures which are ordinarily free from tactile and painful stimulation, and in addition are supplied with a much smaller number of sensory fibers than is the skin. In addition to the deep and poorly localized discomfort which is aroused by appropriate stimulation of the internal organs, as well as of the muscles, ligaments, and other deep somatic structures, pain may be referred to cutaneous areas with a corresponding segmental innervation in the spinal cord by the neurological mechanism of summation of impulses which end in a common neuron pool. It must be borne in mind, however, that this is only a supplementary mechanism and that visceral pain can still be felt after areas of cutaneous reference have been anesthetized.

Careful observation of the area to which pain is referred may be of the greatest value in the diagnosis of visceral disease. Not only should the patient be asked to give an accurate description of the areas to which his pain is referred, but careful examination should be made to map out areas of hyperesthesia, muscle spasm, abnormal sweating or vasomotor changes, and areas of increased pilomotor activity. If these correspond to definite dermatomes, the diseased organ can often be identified from a knowledge of its segmental innervation. If the area of pain corresponds to no recognizable segmental pattern, a diagnosis of hysteria may be seriously considered. Läwen (1923) was the first to use selective paravertebral procaine block of the sympathetic rami and ganglia in the study of the segmental innervation of the viscera. His observations have been corroborated and amplified by surgeons who have resected these structures.

Table II has been compiled from all available data to show the afferent sensory pathways from the various viscera. It is noteworthy that with the exception of the lower colon, bladder, prostate, and uterine cervix, these all enter the cord between the first thoracic and the upper lumbar segments. There is a good anatomical reason for this, inasmuch as no white sympathetic rami are present in the cervical and lowest lumbar segments of the cord. In the following chapters it will be shown that interruption of the appropriate sympathetic rami or ganglia, either by resection or by chemical destruction, can be counted on to abolish visceral pain. The strategic point at which to interrupt the visceral afferent fibers is where their axons are concentrated

TABLE II. THE SEGMENTAL SENSORY INNERVATION OF THE VISCERA

Organ	Superficial Areas to Which Pain Is Referred	Segments at Which Visceral Afferent Axons Enter Spinal Cord																	Peripheral Visceral Pathway
		Thoracic												Lumbar		Sacral			
		1	2	3	4	5	6	7	8	9	10	11	12	1	2	2	3	4	
Heart	Precordium and inner arm	+	+	+	+	?													Middle and inferior cervical and thoracic cardiac nerves
Lung	No referred pain *																		
Liver and Gall Bladder	Right upper quadrant and right scapula						?	+	+	?									Major splanchnic nerve
Stomach	Epigastrium						?	+	+	?									Major splanchnic nerve
Small Intestine	Umbilicus									+	+	?							Major splanchnic nerve
Colon { Ascending	Suprapubic											?	+	+					Lumbar chains and preaortic plexus
Colon { Sigmoid and Rectum	Deep pelvis and anus															+	+	+	Pelvic nerves and plexuses
Kidney	Loin and groin											?	+	+					Renal plexus via least splanchnic nerve and upper lumbar rami
Ureter	Loin and groin													+	+				Renal plexus and upper lumbar rami
Bladder { Fundus	Suprapubic											+	+	+					Superior hypogastric plexus
Bladder { Bladder Neck	Perineum and penis															+	+	+	Pelvic nerves and plexuses
Uterus { Fundus	Suprapubic region and lower back											+	+	+					Superior hypogastric plexus
Uterus { Cervix	Perineum															+	+	+	Pelvic nerves and plexuses

This table, which differs in only minor respects from the one published by Head (1893), has been compiled from all available experimental and clinical data. More recent evidence, which has necessitated minor modifications of Head's original work, is presented in Chapter III and in the clinical chapters of Part II.

* Lung parenchyma is insensitive. Pain from larger bronchi is transmitted over somatic vagal axons. When disease spreads to parietal pleura pain is transmitted over intercostal nerves.

in the paravertebral sympathetic ganglia or the corresponding posterior roots. This rule holds good regardless of whether the pain is assumed to be referred or transmitted directly. Distal to the ganglia the nerves ramify widely, following the course of the visceral arteries, while within the cord the ascending pathways of visceral sensation are not too well understood. Davis, Hart, and Crain (1929) have shown that distention of the gall bladder in dogs is still painful after complete section of the anterolateral column and even bilateral hemisection of the cord at separate levels. This they ascribe to the fact that the ascending visceral pathways run upward within the spinal cord by short fibers with many relays and synapses which have a juxtagriseal position. One of us (White) has frequently observed that after well executed cordotomies sensation on distending the bladder and colon remains intact. It is likely that pain from distention of hollow viscera, as is the case with the sensation of stretching striated muscle or tendon, ascends at least in part in the posterior columns.

The vagus nerve, although a conductor of afferent reflex stimuli such as hunger and vomiting, does not appear to carry pain sensation. If it did, abdominal visceral pain would not be abolished by injuries to the cord or by spinal anesthesia reaching the upper thoracic segments. There are several accounts of surgeons injecting the vagi with procaine in the course of cervical sympathectomies without the slightest effect on angina pectoris, and recently Bradford Cannon (1933) has stimulated the lower vagus in conscious animals by means of buried electrodes without arousing the slightest sign of discomfort.

A number of writers, notably Lehmann (1924), Foerster (1927), and Shaw (1933), claim that some forms of visceral pain enter the spinal cord over anterior roots. Davis (1933) has adequately demonstrated that this exception to the Bell-Magendie law is not valid. He finds that such apparent discrepancies are due to the extensive overlapping of the dermatomes, and that if sufficient posterior roots are cut all forms of sensation are lost.

A final point of interest concerning the rôle of the sympathetic nerves in pain transmission involves their possible regulation of the sensory threshold of the cerebrospinal system. Scrimger (1936) discussed this interesting subject and pointed out that certain people may train themselves to perceive as pain afferent

stimuli from the viscera which do not ordinarily reach the level of consciousness. Continuous or recurring pain may increase its actual perception, so that the sufferer develops all the outward appearance of a confirmed neurotic. It was formerly believed that the autonomic system, which plays such an important rôle in the emotions, may cause alterations in the sensory threshold. Foerster with Altenburger and Kroll (1929, and Altenburger and Kroll, 1930) measured the excitability of the somatic sensory nerves by the determination of their chronaxia. These studies showed that stimulation of the sympathetic chains or the injection of adrenaline raises the sensory threshold, a phenomenon which fits in with the well-known diminution of pain sensation in states of anger and fear. On the other hand, following sympathectomy or the administration of choline or pilocarpine (drugs which stimulate the parasympathetic), the threshold of cutaneous sensation is distinctly lowered. Pette (1927) recorded that frequently after sympathectomy there is paresthesia of the corresponding skin area, and Fulton (1928) observed after lumbar ganglionectomy an increase of cutaneous sensation in the leg. Tournay (1921 and 1925) demonstrated similar results in dogs, and mentioned that in 1851 Claude Bernard described hyperesthesia in the skin of the face and ears of rabbits and cats following superior cervical ganglionectomy.

This evidence of changes in sensory threshold could not be measured with certainty until an accurate sensory stimulus was devised. The difficulty has at last been overcome by measuring pain thresholds in the skin by thermal radiation (Hardy, Wolff, and Goodell, 1940). This method is simple, rapid, and accurate. The threshold of pain is expressed as the number of small calories which must be applied per second to a square centimeter of skin to produce a distinct sense of pain. This figure appears to be surprisingly constant, amounting to only plus or minus 15 per cent from the mean in a series of normal subjects. Dr. W. P. Chapman (personal communication), who is making a study of the sensory threshold in this hospital, has found remarkably little variation in patients with neuralgias and in neurotic individuals. While Hardy, Wolff, and Goodell (1940) found that intense pain in any part of the body raised the pain threshold in other parts as much as 35 per cent, Dr. Chapman has been unable to find any evidence that this is due to the influence of

the sympathetic system. In testing patients before and after various types of sympathetic denervation, he has found no alteration in sensory acuity. Furthermore, he has been unable to demonstrate any alteration of the sensory threshold after injection of either adrenaline or mecholyl.

From the data presented above the rôle of the thoracolumbar and sacral nerves in the perception of pain may be summarized as follows:

1. Sensory axons which conduct pain run in the visceral nerves (proved).

2. Through some mechanism which is still poorly understood (irritable focus) the visceral afferent impulses may also give rise to pain which is referred to the cutaneous areas of the corresponding cerebrospinal nerves (highly probable).

3. By means of axon reflexes the sympathetic fibers may bring about superficial vasoconstriction, contraction of the erector pilae muscles, and possibly a production of irritant metabolites, thereby causing a painful stimulation of the cutaneous sensory nerves (proof uncertain).

4. Evidence that the sensory threshold of the somatic nerves may be altered by the sympathetic nervous system has not been confirmed.

In this general chapter on the physiology of pain many special features which apply to the individual organs have not been included. The discussion of these more specific points is reserved for later chapters which deal with the sensory and motor innervation of individual viscera.

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Chapter VII

METHODS OF STUDY

In this chapter certain apparatus which is desirable for detailed study of vasomotor and sudomotor pathways is described. It is not all essential, however. The three fundamental necessities are a room in which the temperature can be kept constant within 2 degrees or preferably 1 degree Fahrenheit for two hours at a time at any season of the year, an accurate apparatus for the measurement of surface temperature, and a familiarity with methods of producing temporary inhibition of sympathetic activity. Various methods of study are described and an attempt has been made to indicate the relative value and importance of each.

I. Apparatus and Methods

Constant Temperature Room. A room in which the temperature and the humidity can be controlled is of the greatest possible value in investigating patients with vasomotor disturbances.

Accurate temperature control is most important. Slight fluctuations of room temperature are reflected in peripheral surface temperature. Fairly wide variations in humidity, however, have an insignificant effect. A modern operating room which is equipped with temperature and humidity control is a satisfactory place to carry out studies before and after operation.

Differential Thermocouple. Some form of electrical thermometer is essential for rapid and accurate measurement of skin temperature. In the usual form of differential thermocouple two dissimilar metals are in contact with each other, and will be referred to as a junction. When two junctions are exposed to different temperatures a current will flow from one metal to the other in each junction, and from one junction to the other. An electromotive force will thus be produced in the circuit and

will continue to increase with increasing difference in temperature for the range employed in making skin temperature measurements. If one thermal junction consisting of fine copper-constantan wire is applied to the skin and a second is immersed in a bath of known temperature, a deflection will be produced when a delicate galvanometer is placed in series. This deflection corresponds to the temperature difference, and can be readily converted into degrees Fahrenheit or Centigrade. In this book all temperature readings will be given in the Fahrenheit scale. The Tycos Dermatherm, a very practical and portable instrument, is made by the Taylor Instrument Companies of Rochester, N. Y. A self-recording thermocouple-potentiometer, which is capable of measuring the temperature from four different areas simultaneously, is manufactured by the Leeds & Northrop Company of Philadelphia. This instrument is very accurate, eliminates the water junction, and reads directly in degrees Fahrenheit or Centigrade. We have found it to be most satisfactory.

Skin Color Chart. A useful scale of color standards has been published by Sir Thomas Lewis (1929*A*). The primary purpose of this is to allow a given abnormal skin color to be recorded, in order that the degree of blanching or cyanosis may be compared with similar or different skin colors subsequently observed. This scale can be made up by directions published in Lewis's article, and a copy of it should be kept in the room where the examinations of the peripheral circulation are made.

Oscillometer. The oscillometer devised by Pachon is manufactured by Boulitte in Paris. This instrument represents a modified type of plethysmograph which measures in arbitrary degrees the expansile pulsation of an extremity at any desired level. It gives a fairly accurate measure of the pulsation in the main arteries; when these are occluded no oscillation is visible. A more elaborate self-recording form of oscillometer is made by the Taylor Instrument Companies of Rochester, N. Y. Oscillometry is more extensively used in European than in American clinics. Good descriptions of its value for differentiating between vasospasm and arterial occlusion will be found in Leriche's writings. Theis (1937) has given an excellent account of its value in detecting peripheral aneurysms.

Capillary Microscope. By focusing a beam of light obliquely

on skin to which a drop of cedar oil has been applied the capillary loops become visible through an ordinary miscroscope with a low power objective. It is best to use a cooled beam of blue light in order to avoid vasodilatation from heat and to bring out the detail of the capillaries. Using a magnification of 50, the capillaries at the base of the nails can be seen in excellent detail. During vasoconstriction clumps of stagnant erythrocytes can be seen within the capillaries, whereas in phases of vasodilatation they shoot through them so rapidly that they are visible only as a rapid flicker.

By using an adjustable arc lamp and the microscopic camera attachment manufactured by Carl Zeiss, Jena, excellent photographs can be made of the capillaries, showing different pathological conditions and varying states of functional activity. (Fig. 41).

Chamber for Heating the Body. Lewis and Pickering (1931) illustrated a convenient form of chamber in which the patient's body can be heated while the arms protrude and the hands are exposed to a cooler room temperature. We use a very simple cradle which covers the patient's body in bed and raises the temperature up to 125 degrees by incandescent carbon bulbs. This is useful for testing both the sweating reaction and the vasodilator response of the hands or feet exposed to a cool room temperature while the general body temperature is raised.

Syringes and Needles for Injection Tests. The Labat type of syringe and needles, as manufactured by the Anglo-French Drug Company of New York, are most convenient for use in diagnostic procaine tests. The smaller sized 2 and 5 cm. needles are satisfactory for injecting peripheral nerves, while the 8 and 10 cm. needles, which are only 0.9 mm. in diameter, are excellent for injecting the paravertebral sympathetic ganglia.

Determination of Heat Elimination. The Stewart (1911) and Kegerreis (1926) method of determining the calories given off from a given surface area of hand or foot in a calorimeter constitutes an accurate method of measuring the heat elimination of the extremities. Stewart felt that blood flow could be calculated accurately by this method, but Sheard (1927) has pointed out that the conductivity of the skin, the number of functioning capillaries, and other indeterminable factors which vary in different individuals make this impossible. However,

the number of calories given off from each unit area of skin per minute constitutes a good index of heat transfer. Although the method is somewhat difficult, the data on rates of elimination of heat thus obtained are of value from both the physiological and the clinical viewpoints. The method and calculations are well described in Kegerreis's article. It is rather complicated for clinical use.

Direct Estimation of Blood Flow. Freeman and co-workers (1935, 1936, 1937, and 1940) have modified the plethysmographic method of determining the rate of arterial inflow into the hand. This new method is proving to be accurate and of great value for investigative work. The hand is inserted up to the wrist in a special insulated plethysmograph. By passing the wrist through a thin rubber diaphragm and sealing the edges with rubber cement, it is possible to obtain a waterproof seal without in any way impeding the emptying of the veins in the hand. The rubber is reinforced by an adjustable metal diaphragm, and the plethysmograph filled almost to the top with water. Volume changes in the hand are recorded by a Brodie bellows writing on a smoked drum.

To determine the rate of arterial inflow, a sudden venous obstruction is applied at the wrist by the inflation of a narrow blood-pressure cuff from a pressure tank. When the cuff is distended to diastolic pressure, the hand volume increases in a linear manner until the vascular bed is filled; the curve then tapers off to a plateau. From the first part of the curve it is a very simple matter to estimate the rate of arterial inflow and to record it in terms of cubic centimeters of blood per 100 cubic centimeters of hand volume per minute. Readings can be repeated at rapid intervals until they check with a high degree of accuracy. Lampson (1935) used this method to study the effect of smoking upon peripheral blood flow, and found a significant reduction in normal individuals as well as in patients with vascular disease.

This method gives a much better idea of the rate of blood flow than calorimetric measurements. Circulation in the hand can be investigated at any desired temperature. By studying the effect of local temperature on the rate of arterial blood flow, Freeman has shown that the normal hand responds in a characteristic manner. Other equally typical but quite different re-

sponses are found in Raynaud's disease, arterial obliteration, and after complete denervation. Lewis and Grant (1925), Grant and Pearson (1938), and also Kunkel, Stead, and Weiss (1939) have perfected a plethysmographic method of measuring the blood flow and vasomotor reactions in the forearm, leg, and foot.

Arteriography. It is a well-known fact that normal arteries do not cast a shadow on the x-ray plate. Only in arteriosclerosis, where there are extensive deposits of calcium salts in the vessel walls, can they be directly visualized. Even then it is only the main arteries which cast a clear-cut shadow. Therefore, if the entire arterial tree is to be made visible, some radio-opaque substance must be injected. It has been the opinion of physicians at many clinics where special studies have been made of vascular disease that visualization of the arteries by injection of radio-opaque substances is unnecessary and dangerous. Provided a safe method can be found, arteriography will be of great value in the study of difficult cases, and also for the more accurate determination of the results obtained by certain therapeutic measures. Many investigators have sought to perfect a method for its use. In general these methods have involved the use of sodium iodide or iodized oils. The first of these substances has resulted in pain, damage to vessels with gangrene, and occasionally in poisoning and death. The second subjects the patient to the danger of oil embolism. Although Saito and his colleagues (1930) reported its successful use in 130 cases, we cannot overcome our theoretical objections to the injection of oily substances into the blood stream.

Allen and Camp (1932) reported on the use of "Thorotrast" and published some excellent x-rays of the peripheral arteries obtained by its use. Injection of 10 to 25 cc. of this drug causes no pain or injury to the arteries or surrounding tissues, but it is still not definitely known that this amount of thorium dioxide, even with its mild degree of radio-activity, cannot cause ultimate injury to the patient.

Pearse and Warren (1931) used sodium monoiodomethane sulphonate (methiodol) to visualize the arteries of the lower extremities. In their technic the femoral artery was exposed under local anesthesia, and 25 cc. of a 40 per cent solution was injected. The artery was punctured obliquely with a 20 gauge

needle, and compressed proximally during the injection. No untoward effects were noted in either animals or man.

Actual exposure of the artery in question does not seem necessary. Most writers find that the puncture can be made without an incision. There is a general preference for thorium dioxide rather than iodine solutions such as "diodrast," because the latter cause pain and vascular spasm. It is generally agreed that 12 to 20 cc. of "thorotrast" is sufficient to visualize the arteries of the lower extremity and 5 to 10 cc. is adequate for the upper extremity.

In most technics proximal compression of the artery is maintained either by a blood-pressure cuff or by digital pressure. A film is taken after the injection and repeated once or twice after blood flow to the extremity has been re-established for 3 to 6 seconds by release of the compression. Excellent descriptions of technic and illustrations of the use of this method in investigating various types of vascular lesions have been published by Veal and McFetridge (1934, 1935, and 1936), and Allen and Camp (1935). Because of the theoretical objections to the use of radioactive substances and because of the vascular spasm induced by the injection of iodine solutions, we have not found arteriography of much practical value in studying the relation between the sympathetic nervous system and vascular disease.

II. Preoperative Tests

Vasomotor System. There are a number of general considerations which should always be kept in mind while measuring the peripheral circulation by means of surface temperature determinations; otherwise an accurate evaluation will not be obtained. Talbot (1931) has published an extensive study on the skin temperatures of children, which contains a vast amount of interesting data on the reactions of the skin to varying external and internal conditions. To insure the highest degree of accuracy when figures obtained on different occasions are to be compared, a room of constant temperature and humidity is essential. In comparing repeated observations, the tests should be carried out at similar hours of the day and under basic conditions, as Simpson (1931) has shown a diurnal rise and fall in the peripheral circulation. On very hot days, or in the presence of fever or the cachectic state of advanced malignant disease,

normal peripheral vasoconstriction is lost and temperature tests are of no value. In individuals with normal arteries, although there may be fluctuations from hour to hour or from day to day, comparative measurements of symmetrical points on the two sides of the body seldom vary more than 1 to 2 degrees. Therefore when one side is tested with procaine, the opposite extremity serves as a satisfactory control. Figure 30 shows the average comparative temperatures commonly observed in different areas in the limbs and trunk of a normal adult at a room temperature of 76.5 degrees and also when covered up in bed.

A study of the figure cited shows that at ordinary temperatures there is a vasoconstrictor gradient which *increases peripherally* so that the fingers and toes are the coolest points on the surface of the body. The hands and more especially the feet * show a similar cooling of lesser degree, whereas the gradient disappears at the level of the elbows and knees. A possible explanation of this fact may be that the extremities of the body have been exposed to the most extreme variations of temperature during long periods of man's evolution and have therefore developed the most efficient vasomotor control to conserve body heat. When this tonic activity of the sympathetic nerves is eliminated, the temperature gradient in the extremities is abolished and all portions of the body surface reach a nearly constant level. The average maximum vasodilator response for undiseased arteries has been designated by Morton and Scott (1930) as *"the normal vasodilatation level."* The lower limit of this level in extremities whose vasoconstrictor nerves have been released by general or regional anesthesia, or by elevating the body temperature, may be taken at 86.5 degrees Fahrenheit. Our experience leads us to believe that the surface temperature at the tips of the digits should rise to 90 degrees Fahrenheit or more when the room temperature is 68 degrees. If this does not occur following inhibition of sympathetic activity, we suspect the presence of organic vascular disease.

The fundamental factor in the quantitative estimation of the activity of the vasoconstrictor nerves is not the total rise in tem-

* This is particularly true at the time of a test, as the emotional reaction is sufficient to set up a reflex increase in vasoconstrictor tone and thereby to cause "cold feet," literally as well as figuratively.

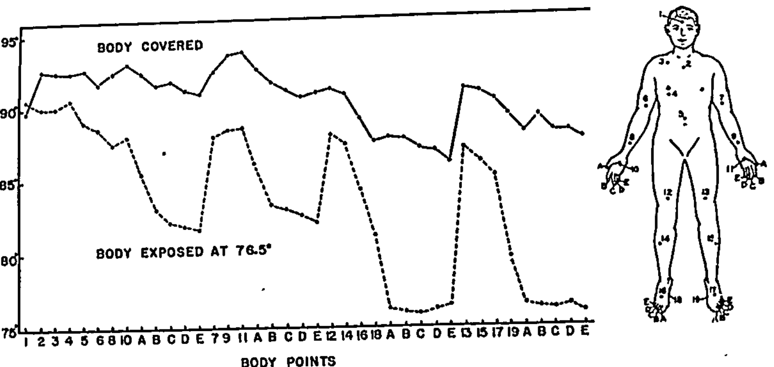


FIG. 30. Average skin temperatures in various parts of the body.
(Redrawn from Coller and Maddock, *Annals of Surgery*, 1932, XCVI, 719, with permission.)

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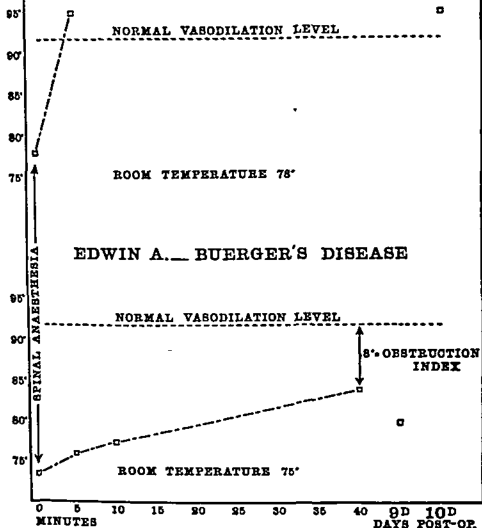


Fig. 31. Spinal anesthesia test.

The upper chart shows the surface temperature response in the toes in a case

as the simplest method of estimating the vasodilator response. Sir Thomas Lewis (1929*B*) had previously utilized ulnar nerve block at the elbow to study the rise of temperature in the little finger. All of these methods temporarily paralyze the vasomotor impulses and give a quantitative measure of the elevation in

perature of a given digit, but how nearly the rise approaches the normal vasodilatation level. The former response may depend on the initial coolness of the extremity, while the latter is a measure of the completeness of arteriolar dilatation. If the maximum surface temperature recorded in a given patient is subtracted from the normal vasodilatation level, an index of the amount of arterial occlusion is obtained (Fig. 31). In the typical early case of Raynaud's disease the skin temperature reaches the vasodilatation level, but if the disease is advanced and sclerodermatous changes have produced a constricting fibrosis about the digital arterioles, the resulting vasodilatation may fall far short of the normal level. While the advanced arteriosclerotic cannot be expected to show any appreciable elevation in peripheral temperature, many early cases of thromboangiitis obliterans submitted to the tests respond with a striking degree of vasodilatation.

We have found it useful to make peripheral surface temperature charts of each patient after exposure for one hour to a room temperature of 68 degrees Fahrenheit, with the trunk covered in a standard manner while the extremities are exposed to the room temperature. Typical charts are illustrated in Chapter VIII (Figs. 45, 46, and 47).

There are four common methods of differentiating between arteries which are constricted by spasm and those which are narrowed by disease:

a. Diagnostic Procaine Block. In 1930 (*A* and *B*) White reported that the sympathetic vasomotor fibers could be blocked temporarily by procaine as effectively as by actual operative methods. These articles showed that maximal vasodilatation can be accomplished either by paralyzing the sympathetic fibers in the anterior spinal roots (spinal anesthesia), by infiltrating procaine around the sympathetic ganglia and their communicant rami (paravertebral block), or by infiltration of the postganglionic neurons in the mixed spinal nerves (peripheral nerve block). A few weeks preceding the publication of this paper Brill and Lawrence (1930) reported the use of spinal anesthesia for this purpose, and shortly thereafter Morton and Scott (1930) published further studies showing the value of spinal block for measurements in the lower extremity. Later they advocated blocking the peripheral nerves (*posterior tibial, ulnar, or median*)

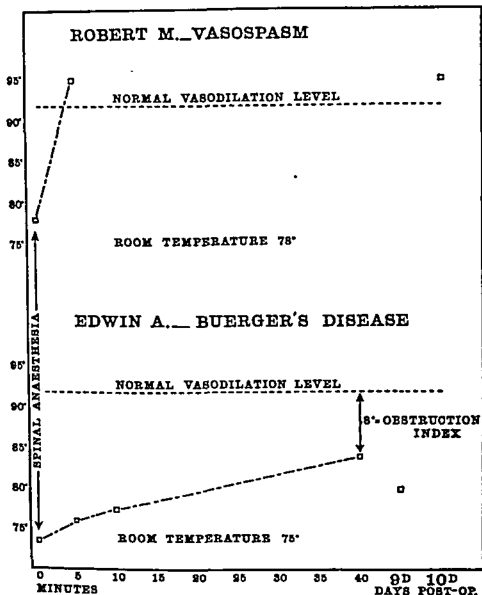


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peripheral temperature which can be expected to follow sympathectomy.

The various forms of sympathetic paralysis with procaine are accurate quantitative measures of the degree of vasodilatation that will result from operation.* These procedures are relatively easy for anyone to carry out who is experienced in the use of regional anesthesia. Peripheral nerve block and even injection of the sympathetic ganglia cause distinctly less discomfort to the patient than the febrile response induced by typhoid vaccine. We feel also that the injection methods are safer than foreign protein shock, as we have had no troublesome complications in a series of several hundred cases. In the opinion of all the members of our peripheral vascular clinic the procaine test is the most satisfactory and accurate method of selecting cases of Raynaud's and Buerger's disease for sympathectomy.

The technic of performing these injections is very well described in Labat's textbook (1930) and also in articles by White (1930*A* and *B*), Morton and Scott (1930 and 1931), Flothow (1931), and de Takats (1931). In performing the diagnostic spinal injection it is best to have the patient lie on his side and to inject slowly into the fourth lumbar interspace 100 mg. of procaine crystals dissolved in 3 cc. of spinal fluid. A typical response to this injection in the case of Raynaud's disease is shown in Figure 31. The lower curve illustrates the slower and less striking response obtained in a patient with thromboangiitis obliterans who showed a definite degree of vasconstrictor spasm, and was later subjected to lumbar ganglionectomy as a result of this test.

In carrying out paravertebral injection of the stellate ganglion, 5 cc. of 2 per cent procaine-adrenaline is injected against the sides of the first and second thoracic vertebrae. The technic of this is described on page 443 (Figs. 86–88). Procaine injected in this region will diffuse freely through the retropleural areolar tissue, infiltrating the spinal nerves, the communicant sympathetic rami, and the ganglionated chain. Blocking these structures results in Horner's sign, cessation of perspiration, and

* Although the immediate effect of operation checks up exactly with that [illegible] turn [illegible] ted [illegible] ear

P V. BLOCK. NOVOCAINE. T_3 LEFT.
T_2 "
HORNER'S SYNDROME +++
HORNER'S SYNDROME ++
HORNER'S SYNDROME 0
100°
90°
80°
ROOM TEMP.
70°
TIME 9^{00} 9^{15} 9^{30} 9^{45} 10^{00} 10^{15} 10^{30} 10^{45} 11^{00}
3RD FINGER LEFT
" " RIGHT

Fig. 32. Results of paravertebral procaine injection in a patient with uncomplicated vasospasm.

vasodilatation in the arm and corresponding side of the face (Fig. 32).

Following infiltration of any peripheral nerve there results a vasomotor paralysis over the area of anesthetized skin. For testing the vascular responses in the foot the simplest method is to inject the posterior tibial nerve at the internal malleolus (Fig. 33) (Morton and Scott, 1931). In the hand vasodilatation can be easily produced by blocking the ulnar nerve at the elbow (Lewis, *1929B*) (Fig. 34). In several instances of severe Raynaud's disease where we have injected the ulnar nerve alone we have failed to obtain complete vasodilatation of the little finger, but by injecting the median as well, a more complete response may be elicited.

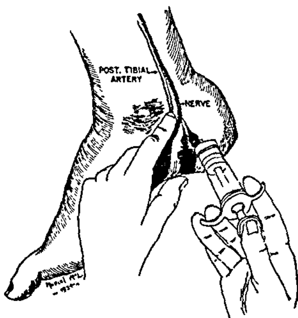


FIG. 33. Posterior tibial block behind internal malleolus.

b. General Anesthesia. Most general anesthetics cause vasodilatation throughout the entire cutaneous area comparable to the regional effect of procaine block of the sympathetic ganglia or the mixed peripheral nerves. Scott and Morton (1930) described this phenomenon under anesthesia with ether, nitrous oxide-oxygen,* and tribromethyl alcohol. It is also a common observation that even mild alcoholic intoxication causes a striking degree of vasodilatation in the skin. Under these circumstances the organism loses its capacity to conserve heat and the temperature of the blood slowly falls.

* [illegible] pressure.

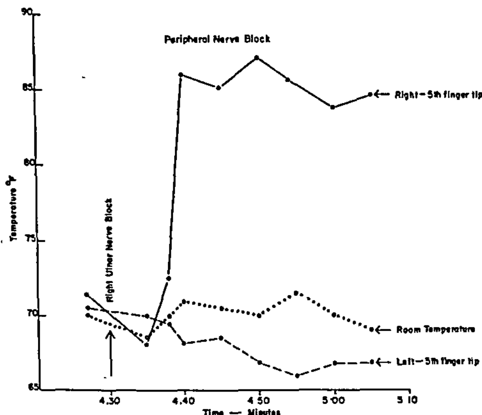


Fig. 34. Diagnostic ulnar nerve block at elbow.

Typical response to diagnostic peripheral nerve block in a patient with Raynaud's phenomenon and early scleroderma. Note failure of surface temperature to reach or exceed 90 degrees Fahrenheit. This is one of our criteria for determining the presence or absence of local fault. Unless the procaine is actually injected within the nerve, the response may be delayed and incomplete. Motor and sensory paralysis should be complete within five minutes.

Figure 35 shows the variation in surface temperature during induction, full surgical anesthesia, and recovery from ether anesthesia. Under these circumstances the vasoconstrictor gradient is abolished as soon as a depth of anesthesia is reached which produces moderate muscular relaxation. Under gas-oxygen there is an actual vasoconstriction during the period of struggle, so that in some cases ether may have to be added to induce an adequate paralysis of vasomotor as well as of striated muscle tone.

Because the induction of and recovery from a general anesthetic are obviously more disagreeable to patients than are other diagnostic methods, this test should be used only under special circumstances. In clinics where no expert in regional nerve

block is available general anesthesia can be of value when the foreign protein and the body heating tests (see below) have given indeterminate results. We have also utilized it occasionally in straightforward cases of Raynaud's disease where it was nearly a foregone conclusion that there was no element of

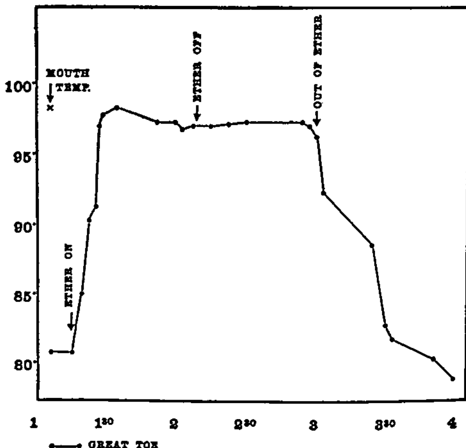


FIG. 35. Vasodilatation under ether anesthesia.

arterial occlusion. Such patients have been anesthetized with gas-oxygen ether, the rise in skin temperature checked while the patient was being transferred to the operating table, and sympathectomy performed immediately thereafter. Under these circumstances the diagnostic test can be combined with operation at the cost of only a few minutes' delay.

c. Peripheral Vasodilatation by Heating the Body. Pickering (1932) has shown that when the temperature of the blood

is elevated as little as from 0.018 to 0.072 degrees Fahrenheit (0.01 to 0.04 degrees Centigrade) vasodilatation occurs in the skin through the action of the central heat-regulating mechanism. A number of extremely simple and useful tests based on this fundamental principle have been developed for the differentiation of vasospasm from arterial obliterative disease.

Lewis and Pickering (1931) illustrate a cabinet in which the patient's body is heated to 125 degrees by means of electric light bulbs, while the head and arms protrude into the colder atmosphere of the room (68 degrees). As soon as the body within the heated cabinet begins to perspire the patient without arterial occlusion responds by a rapid warming of the hands to the normal vasodilatation level. We use a different form of heating box which enables us to expose either the arms or legs. Responses in patients with Raynaud's disease and arteriosclerosis are usually identical with those previously illustrated after procaine injection. In cases where an unexpected reaction is obtained the response should be verified with procaine.

Gibbon and Landis (1932) utilize this principle of heating the blood by having the patient sit with forearms or legs immersed in hot water (110 to 112 degrees) while the extremities to be tested are exposed to the cool atmosphere of the room. In patients with vasospasm dilatation of the vessels in the skin begins in fifteen minutes and should be complete within a half-hour.

All these body heating methods are extremely simple and necessitate no expensive apparatus except the thermo-electric thermometer, which is indispensable to any clinic undertaking this form of surgery. Whichever one appeals most to the individual surgeon should be developed as his routine test, so that he may become thoroughly familiar with it. It should be realized, however, that at times the response is not clean cut. Whenever there is the least uncertainty the patient should be tested again by one of the methods of procaine block, which remain the most accurate means of studying vasomotor activity at our disposal.

d. Foreign Protein Injection. In 1926 Brown devised the first practical method of differentiating conditions of circulatory deficiency in the extremities due to vasospasm of nervous origin (Raynaud's disease) from organic occlusion of the arteries (ar-

teriosclerosis and thromboangiitis obliterans). This method consists in producing an artificial fever by the intravenous injection of foreign protein and measuring the vascular response in the extremities during the period of the reaction. Brown suggested the use of typhoid vaccine for this purpose. Our experiences with this method have been summed up by Allen and Smithwick (1928). It has been our practice to inject 50,000,000 killed typhoid organisms into a vein and to observe the subsequent changes in skin temperature, color, and at times the changes in blood flow through the capillary microscope.

In order to follow these changes under basic conditions the test should be carried out in a room where the temperature can be maintained relatively constant, and the extremities of the patient should be exposed for half an hour preceding the test. Readings are recorded before the injection and thereafter at half-hourly intervals during the rise and fall of the febrile reaction. Characteristically, the patient complains of chilly sensations, or an actual shaking chill, some two to three hours after the injection. During this period the vasomotor nerves cut down loss of heat from radiation by intense constriction of the superficial vessels and thereby produce a fever. There result a definite fall in surface temperature, color changes ranging from pallor to cyanosis in the extremities, and nearly complete capillary stasis (Fig. 36). In the case of a patient with definite arterial obliterative disease it is essential to reduce this intense spasm by the application of artificial heat. Otherwise actual thrombosis may occur in the vessels which are already partly occluded. At the moment when the body temperature begins to fall the reverse of this phenomenon takes place; in cases where organic arterial occlusion is slight or absent vasoconstriction is replaced by vasodilatation. The extremities become pink and skin temperature rises rapidly. There is a tremendous increase of circulation in the capillary loops, through which clumps of red cells pass with such rapidity that they are barely visible. Profuse sweating occurs at the same time. By this mechanism the autonomic nervous system causes a fall in body temperature through radiation of heat and further cooling by perspiration and evaporation.

The foreign protein test can be simplified by taking only two readings of the skin temperature, first in the normal state and

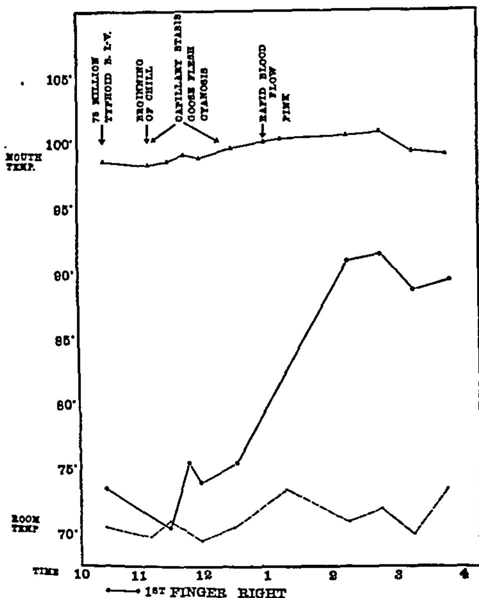


FIG. 36. Foreign protein reaction in a case of uncomplicated vasospasm. Vasomotor index = 5.

secondly at the time the mouth temperature begins to fall. In routine tests, after preliminary skin temperature measurements and the injection of the vaccine, half-hourly mouth temperatures are taken by the nurse. At the time the patient begins to feel chilly he is wrapped up in blankets and hot-water bottles are applied to his hands and feet. As soon as the mouth temperature has reached a plateau or begins to fall, the extra blankets and hot-water bottles are removed and the hands and feet

again exposed to room temperature. A half-hour later the final skin temperature measurements are taken.

The important features of this test are expressed in Brown's vasomotor index, a factor which expresses the number of degrees the surface temperature rises for each degree of elevation in the temperature of the blood. This may be expressed in the formula:

$$\frac{\text{Rise of peripheral skin temperature} - \text{Rise of mouth temperature}}{\textit{Rise of mouth temperature}} = \text{Vasomotor index.}$$

In a typical case of Raynaud's disease (Fig. 36) the peripheral temperature may rise 5 to 10 times as much as the general temperature of the body, giving figures of the following order:

$$\frac{\text{Rise of skin temperature } 18^\circ - \text{Rise of mouth temperature } 3^\circ}{\text{Rise of mouth temperature } 3^\circ} = \frac{15}{3} = \text{a vasomotor index of 5.}$$

Thus this equation shows that vasodilatation has caused a rise of skin temperature 5 times greater than the general rise in body temperature.

In a case of arteriosclerosis where there is pure vascular occlusion without any element of vasospasm, figures of the following type are commonly obtained:

$$\frac{\text{Rise of skin temperature } 6^\circ - \text{Rise of mouth temperature } 5^\circ}{\text{Rise of mouth temperature } 5^\circ} = \frac{1}{5} = \text{a vasomotor index of 0.2.}$$

In cases of thromboangiitis obliterans the impairment of circulation may be entirely due to vascular occlusion. On the other hand, a greater or lesser degree of vasomotor spasm is frequently present as well. Under these circumstances the vasomotor index would be definitely greater than in the typical arteriosclerotic, but never as high as in the case of Raynaud's disease. Whenever the vasomotor index exceeds 2, Adson and Brown (1932) feel that sympathetic ganglionectomy will cause a worth-while permanent rise in surface temperature.

This method is at best a qualitative test. The rapid and often intense febrile reaction is extremely disagreeable to the patient, and in cases of advanced vascular occlusion is distinctly dangerous. Several instances of massive thrombosis and gangrene

have followed its use. With the development of more recent methods, the foreign protein test has been generally discarded.

Localization of Viscerosensory Pathways by Diagnostic Injection. Paravertebral injection of the sympathetic ganglia with procaine is just as applicable to the study of afferent nerve pathways as it is to the quantitative determination of vasomotor activity. Läwen (1923) and von Gaza (1924) first utilized this as a diagnostic aid in the investigation of the pathways of visceral pain. By its use Mandl (1925) was able to define more exactly the afferent cardiac nerves. In this country, however, little attention was paid to these excellent articles before the reports of Archibald (1928) and Scrimger (1929). Since the publication of their papers an increasing appreciation of the diagnostic value of this procedure has been shown by frequent reports in the surgical journals. From the Massachusetts General Hospital, White (1930*A* and *B*) and Mixter and White (1931) have shown its value in neurological localization in unusual forms of vascular and visceral pain. Valuable papers describing its application and uses have been written by Woodbridge (1930), Alvarez (1931), Flothow (1931), Abbott (1932), Livingston (1938), and Homans (1940).

Before discussing the technic of diagnostic injection for the study of visceral pain it is necessary to warn against its indiscriminate use in obscure painful conditions. All other diagnostic and therapeutic methods must be tried first. A lumbar puncture must always be performed to make certain that there is no disease of the spinal cord. In older patients it is also best to take x-rays of the vertebrae to rule out spinal arthritis and metastatic malignancy. The opinion of an experienced psychiatrist is often of great value in the difficult differentiation between obscure visceral pain and a psychoneurosis. It must be remembered that many of these cases have the characteristics of the neurasthenic, because prolonged suffering and the frequently associated addiction to drugs lower the sensory threshold as well as the patient's morale. When incurable visceral disease, such as aneurysm of the aorta or carcinoma of the stomach, is the cause of pain and the only problem is to discover the pathways of its transmission and the best way to interrupt them, procaine injection is indicated from the start.

The technic of injection for the study of intractable pain dif-

again exposed to room temperature. A half-hour later the final skin temperature measurements are taken.

The important features of this test are expressed in Brown's vasomotor index, a factor which expresses the number of degrees the surface temperature rises for each degree of elevation in the temperature of the blood. This may be expressed in the formula:

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This method is at best a qualitative test. The rapid and often intense febrile reaction is extremely disagreeable to the patient, and in cases of advanced vascular occlusion is distinctly dangerous. Several instances of massive thrombosis and gangrene

relieved as soon as procaine is added, then the chances are all in favor of permanent relief following sympathectomy or a successful injection of alcohol.

It is obvious that these methods are trying, both to the patient and to the surgeon, yet any amount of effort on the part of the latter, and even a considerable degree of discomfort to the former, are better than a useless operation.

In the case of pain from the head, arm, or leg the sympathetic innervation to these regions can usually be blocked without anesthetizing their somatic sensory nerves, as these principally enter the cord cephalad or caudad to the thoracolumbar white rami. In the thorax and abdomen, however, infiltration of procaine around the sympathetic ganglia results in a simultaneous anesthesia of the corresponding spinal nerves. In these situations it must be recalled that pain arising in the parietal pleura or peritoneum, as well as in other parts of the thoracic or abdominal wall, can be relieved only by section of the posterior roots or the spinothalamic tract. Pain in the viscera themselves is entirely interrupted when the correct visceral afferents which run in the sympathetic trunks are blocked, and relief is sure to follow resection of these ganglia or their destruction with alcohol.

The application of this method to the study of various specific types of visceral pain will be taken up in detail in later chapters.

III. Postoperative Tests to Determine the Completeness of Sympathectomy or Evidence of Regeneration

Sweating Tests. When the peripheral sympathetic neurons are paralyzed, spontaneous activity of the sweat glands ceases in the sympathectomized region. This subject has been discussed in detail by List and Peet (1938*A*,*B*,*C*, and *D*) and by Roth (1937). After cervicothoracic ganglionectomy the area of anhidrosis generally involves the corresponding side of the head, the arm, and the upper thorax down to the region of the second or third ribs. When the second to fourth lumbar ganglia have been removed, sweating disappears at a variable point between the groin and knee. This is a simple and effective way of demonstrating the completeness of sympathetic denervation (Fig. 37).

fers in no way from that of diagnostic paravertebral procaine block in vasomotor conditions. Selective blocking of the visceral afferent nerves is of particular value in localizing the segments over which pain is referred, and in deciding whether it can be permanently interrupted by sympathectomy or should be attacked by more radical procedures on the spinal cord. The test is also a great assistance in differentiating individuals with true visceral pain from the psychoneurotic group.

In cases of abdominal pain of unknown origin a useful preliminary method of localization has been suggested by Alvarez (1931). This consists in administering a high spinal injection of procaine and in determining the level of skin anesthesia at the moment the pain disappears. In the case of the neurotic patient, total anesthesia of the trunk may have no effect on the patient's sensation of pain. In the real sufferer, however, the pain characteristically ceases as anesthesia reaches a certain segment and reappears at the same level when it wears off.

Other clues to the segments over which visceral pain enters the spinal cord can be gained from observation of areas of skin hyperesthesia or abnormal sweating, as well as from a knowledge of visceral innervation (Table II). Pain referred to the right upper quadrant may arise from the biliary passages; under these circumstances it can be interrupted by blocking the seventh to ninth thoracic ganglia. If the pain comes from the region of the kidney, injection of the twelfth thoracic and upper two lumbar ganglia will interrupt it. It is important to limit the amount of procaine injected in the region of any ganglion to 3 cc., since large amounts may spread over a wide area and give very misleading results. If the injection of two to four ganglia is unsuccessful, the process should be repeated at a later date and at a higher or lower level. Even if successful, the test should be repeated and verified on several occasions. So great is the power of suggestion in the neurotic type of patient, that the pain may be temporarily relieved because the patient feels that something dramatic is being done to him. An operation performed on such a false premise will certainly fail to benefit or may even aggravate the pain. In order to rule out the psychoneurotic and the malingerer, inert salt solution instead of procaine should be injected at the beginning of one of the tests without the patient's knowledge. If this fails to influence the pain, but the patient is

level of skin resistance is dependent upon sweat gland activity, it is always much higher after complete sympathectomy. Furthermore, it is constant in level, and reflex responses to noises or physic influences are abolished. A psychogalvanometer is used for this test. It is probably the most sensitive method of all for determining completeness of sympathetic denervation, and for detecting the earliest signs of regeneration. It is, however, too complicated for general clinical use. The changes before and after sympathectomy are illustrated in Figure 50 (Chap. VIII). Detailed discussion of the galvanic skin reflex can be found in the writings of Darrow (1929), Richter (1929), and Landis (1932).

Reflex Vasomotor Responses. Any of the methods previously described for inhibiting vasoconstriction or promoting vasodilatation can be used to demonstrate the presence or absence of intact vasomotor pathways after operation or to detect evidences of regeneration. These are heating the trunk with a cradle, immersion of the opposite extremities in hot water, or covering the body with blankets. None of these methods is well suited for the detection of minor variations in surface temperature.

More sensitive is the photoelectric cell (Hertzman, 1937 and 1938; Finesinger *et al.*, 1939; Smithwick, 1940*A*) or the finger plethysmograph (Bolton, Carmichael, and Stürup, 1936). The latter in our experience is more sensitive than the former in detecting early evidence of regeneration or slight degrees of incompleteness of sympathetic denervation. Reflex changes in response to various stimuli detected by the photoelectric cell are illustrated in Figure 51 (Chap. VIII). Some sensitive method of studying vasomotor activity should be employed to prove complete denervation or detect regeneration. With minor exceptions the absence of reflex sweating and abolition of the galvanic skin reflex proves that vasomotor pathways are completely interrupted.

Procaine Hydrochloride Block. If the effect of operation is incomplete or if regeneration has occurred, blocking sympathetic pathways with procaine (as in the routine preoperative test) will result in a significant rise in surface temperature. Peripheral nerve block is by all means the simplest method, injecting the ulnar nerve at the elbow in the case of the hand (Fig. 34). In testing the lower extremity the posterior tibial

A satisfactory way of testing for paralysis of the sudomotor nerves is to place the patient in an electrically heated cabinet at a temperature of about 125 degrees until there is profuse perspiration over the normal areas of skin. Other clinics have advocated the use of pilocarpine nitrate, 1/20 grain (3 mg.), injected subcutaneously with repetition of the dose until generalized profuse sweating and salivation result. We believe that this test is unnecessarily disagreeable to the patient. In addition it is frequently inaccurate, as large doses can still cause sweating in the denervated areas by direct action on the secretory cells (Burn, 1925; Guttmann, 1931).

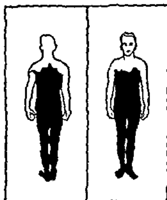


FIG. 37. Reflex sweating test

After bilateral preganglionic thoracic sympathectomy there is complete anhidrosis of the head, upper extremities, and thorax to T_4. Below this level normal or increased reflex sweating is indicated by the iodine starch reaction.

While moderate degrees of sweating are visible or can be made out by sense of touch, there are two simple chemical methods for detecting the slightest secretion:

a. Cobalt Blue Papers. Sheets of filter paper are dipped in cobalt chloride solution and dried on a steam radiator. When dry they are blue,* but when even slightly damp their color changes to pink. These can be laid over the areas to be tested and attached to the skin with adhesive plaster.

b. Starch-Iodine Test (Victor Minor, 1928). To 900 cc. of dilute tincture of iodine (1.5 per cent) 100 cc. of castor oil are added. This solution is painted on the skin and after evaporating leaves a thin film of oil and iodine. Starch powder dusted over the area adheres to the oil and wherever any moisture appears turns a deep blue-black color. One advantage of this test is that the area of sweating stands out clearly on the photographic plate (Fig. 37).

Reflex Changes in Cutaneous Resistance. A study of cutaneous resistance offers another extremely sensitive method for demonstrating interruption of sudomotor pathways. Because the

* Pink $CoCl_2 \cdot 6\ H_2O$ forms the blue anhydrous salt on giving up its water of crystallization.

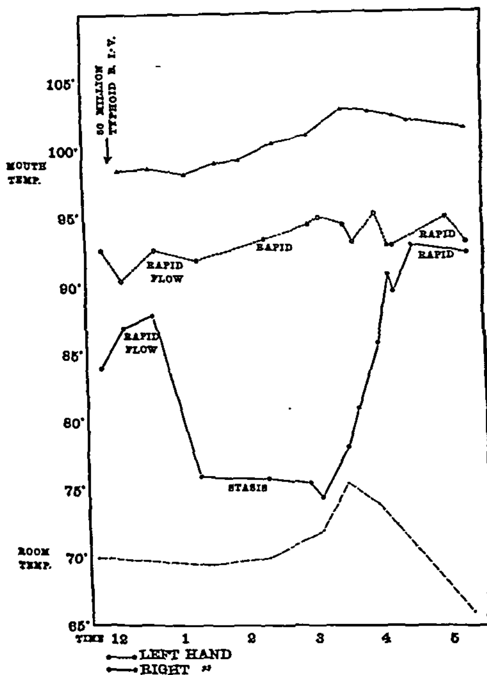


FIG. 38. Foreign protein reaction in fully sympathectomized (left) and normal (right) extremities.

nerve can be blocked at the internal malleolus and the common peroneal at the head of the fibula. For general use, the combination of postoperative peripheral nerve block and the reflex sweating test is adequate for demonstrating completeness of denervation or for detecting evidence of regeneration (Simmons and Sheehan, 1937 and 1939; Smithwick, 1940*B*).

Pilomotor Tests. The erector pilae muscles in the hair follicles are composed of smooth muscle and are innervated by the sympathetic. When this system is paralyzed "goose-flesh" can no longer be produced spontaneously. Simple methods of eliciting the pilomotor reflex consist of applying ice to the patient's spine, or sudden immersion in a hot bath. It may also be produced directly by stimulating a local area of skin with faradic current through a bipolar electrode, as described by Lewis and Marvin (1927). While the reflex response disappears when any portion of the reflex arc is destroyed (somatic sensory nerve, pre- or postganglionic neurons), the response to direct stimulation disappears only when the postganglionic neurons have degenerated. Thus no pilomotor reflex can be evoked in either the arm or hand after cervicothoracic ganglionectomy, but the direct response will still be present when the upper extremity is denervated by preganglionic section.

Foreign Protein Response. It has been pointed out in the section on preoperative tests (page 164) that the intravenous injection of typhoid vaccine produces a preliminary vasoconstriction during the period of rising temperature, followed by full vasodilatation during the subsidence of the fever. In a fully sympathectomized extremity there is no visible change in capillary blood flow and only a slight elevation in the skin temperature which parallels the increased temperature of the blood. Figure 38 shows the characteristic response in sympathectomized and control extremities.

Adrenaline Test. In Chapter V it has been demonstrated that as the sympathetic nerves to a part degenerate the denervated smooth muscle of the arteriolar walls becomes hypersensitive to adrenaline. As a result, injection of 1 part adrenaline in 250,000 parts of normal saline (injected intravenously at the rate of 40 to 60 drops per minute) will cause striking vasoconstriction in extremities after complete degeneration of their sympathetic nerves. This response is maximal after a postganglionic opera-

This is accompanied by the sudden onset of sweating, color changes, and coolness of the extremity. This phenomenon may be marked or slight. The change is usually noticed by the patient and may be so marked that it makes one wonder if the extremity in question was really denervated. These signs disappear after thirty-six to forty-eight hours. If peripheral nerve block is done during this phase, a rise in surface temperature of as much as 10 degrees Fahrenheit may be detected. A number of patients have been studied during this phase. Although skin resistance is temporarily reduced, reflex variations in resistance and vascular responses are absent. This suggests that spontaneous activity arises in the decentralized sympathetic ganglia.

If one makes repeated measurements of sensitivity to adrenaline it will be seen that this sensitization phenomenon makes its appearance about the end of the first week after operation, and reaches its height at the end of the second or beginning of the third week. Thus it is evident that important changes are taking place during the first fortnight. During the third week there is a slight, gradual fall in surface temperature and skin resistance. Finally, by the end of this period, the extremity becomes stabilized and no further changes take place unless regeneration occurs or vascular disease progresses. Therefore, it is unwise to make postoperative studies for future comparison earlier than three weeks after operation. At this point the surface temperature is never quite as high as it is the day after sympathectomy. Procaine block may reveal a 1 or 2 degree rise in surface temperature, due to slight residual innervation or the result of continued discharge from decentralized ganglia. It is of no clinical significance. The curious phenomena noted in the early weeks after sympathectomy have been discussed in greater detail by Smithwick (1940*A*).

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tion and still present, but greatly reduced, after a preganglionic denervation. In the normally innervated skin or after an inadequate operation it is minimal, unless excessive amounts of adrenaline are used or the drug is injected intra-arterially, as reported by Fatherree, Adson, and Allen (1940).

IV. Changes after Sympathectomy

Certain phases through which an extremity passes after preganglionic denervation deserve a word of comment. If daily surface temperature and skin resistance readings are taken one will detect certain variations during the first three weeks. These

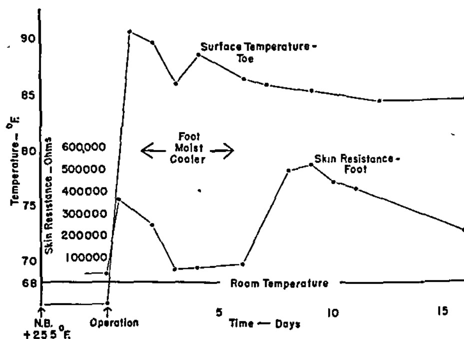


FIG. 39 Surface temperature and skin resistance changes after preganglionic sympathectomy

Daily surface temperature and cutaneous resistance readings, plotted for two weeks after complete denervation of the lower extremity. The curves are similar to those noted for the upper extremity. The phase of lowered temperature and cutaneous resistance levels accompanied by clinical evidence of moisture and coolness is brought out (From Smithwick, 1940*A*, courtesy of *Archives of Surgery*)

are illustrated in Figure 39. The preliminary high level of surface temperature and skin resistance which is maintained for the first few days after operation undergoes a curious depression which occurs, as a rule, from the third to the fifth or sixth day.

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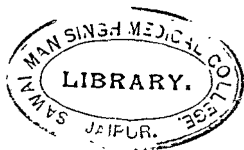
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PART II



INTRODUCTION

The chapters in Part II take up those conditions in which it is possible to modify abnormal activity on the part of smooth muscle and glands by destruction of their autonomic nerves. Visceral pain, from the fact that the afferent visceral neurons (somatic) run in the autonomic trunks, is treated as a subject of equal importance. While it is seldom feasible to resect the sympathetic nerves to one organ, like the lower bowel, selectively, a thorough knowledge of neurophysiology makes it possible to spare the important neurons to the neighboring viscera. As a result sympathectomies in properly selected cases, when scrupulously performed, may be extremely satisfactory. The purpose of this section is to point out those conditions which are suitable for sympathectomy and equally those which are not. No particular effort will be made to discuss the purely medical aspects of these diseases nor their differential diagnoses, as this would constitute a useless repetition of textbooks on general medicine and neurology. It will be noted that the antiquated doctrines of sympathicotonia and vagotonia are never mentioned. Furthermore, there is no chapter on tumors. With the rare exception of paroxysmal hypertension from a secreting adenoma of the adrenal medulla, these neoplasms produce no specific physiological phenomena and are therefore of no particular interest in this field. They are best described in the texts on neoplastic disease.

severe cases go on to dry gangrene of the phalanges. The spasm is intermittent and occurs on exposure to cold or emotional stimuli; it involves only the terminal arteries, while the main vessels continue their normal pulsations. Frequently these patients complain of excessive perspiration, which is also limited to the extremities. The disease most commonly occurs in young individuals with hyperirritable nervous constitutions."

While wishing to exclude all instances of primary obliterative disease of the arteries from this discussion, we can see no purpose in differentiating between classical Raynaud's disease described above, and such allied vasospastic conditions as acrocyanosis. In the former cyanosis alternates with pallid asphyxia, while in the latter the extremities are constantly blue, as well as abnormally cold. Both conditions have a common underlying cause and both can be relieved surgically by cutting the vasoconstrictor pathways. For these reasons acrocyanosis will be considered in this chapter on the vasomotor disorders as a variety of Raynaud's disease and not as a separate clinical entity.

Examination of the peripheral circulation of a large number of normal individuals will disclose occasional cases of excessively cold, moist hands and feet (Fig. 45). An excellent example of this condition drawn from fiction is Dickens' Uriah Heep.* All of us are acquainted with such individuals and if we observe them closely will note that their hands become dusky to cyanotic in the cold. When they grasp a cold object like the steering wheel of an automobile on a cold day their fingers may become abnormally white. During the winter months they are forced to wear bed socks at night, and even then may have difficulty in keeping their feet warm. Characteristically these are young, emotional individuals, and most frequently women. Ordinarily they complain of "poor circulation" and make the best of this handicap. Most often this condition does not advance, but rather diminishes with increasing age and the general reduction in sympathetic activity that goes with it. However, in following a number of these individuals over a period of years we have seen some progress to typical full-fledged Raynaud's disease. It has

* *David Copperfield*, Chapter XVI: "I found Uriah reading a great fat book, with such demonstrative attention, that his lank forefinger followed up every line as he read, and made clammy tracks along the page (or so I fully believed) like a snail. . . . It was no fancy of mine about his hands, I observed; for he frequently ground the palms against each other as if to squeeze them dry and warm, besides often wiping them, in a stealthy way, on his pocket-handkerchief."

Chapter VIII

THE SYMPATHETIC NERVES IN PERIPHERAL VASCULAR DISEASE

I. Raynaud's Disease and Allied Vasomotor Disorders

Definition. In 1862 Maurice Raynaud described a disease entity characterized by symmetrical impairment of the circulation in the fingers and toes with phasic color changes, a condition which often progressed to ulceration of the finger tips and gangrene without occlusion of the larger arteries. His early description, in which he segregated this syndrome from a large group of peripheral gangrenes concerning which little was known, has become a medical classic. His observations were so complete and his deductions from them so judiciously drawn that little was added to them in the next sixty years. The disease has appropriately come to be called by his name. His two articles (1862 and 1874) should be read in full by all who are interested in peripheral vascular disease.*

In many past and current articles the term Raynaud's disease has been loosely applied to a great variety of circulatory disorders † In order to exclude extraneous conditions the following definition has been formulated by the peripheral vascular clinic of the Massachusetts General Hospital:

"Raynaud's disease is a form of peripheral vascular disturbance caused by tonic contraction of the smaller arteries in the extremities. During the early uncomplicated stages of the disease there' are no obvious pathological changes in the walls of the arteries The disease commonly involves symmetrical areas in the hands and feet, causing circulatory stasis with periods of cyanosis or pallid asphyxia. The

* [illegible] available, published by the [illegible]

† [illegible] litions which lead to sym- [illegible] Lewis and Pickering. This [illegible]

discoloration disappears rapidly on warming. The attacks of dead white blanching of the skin occur later in the disease. These periods of total syncope are seen much more frequently in the fingers than in the toes. They begin symmetrically in the finger tips of both hands and spread to involve the full length of the fingers. The thumbs may or may not be involved. In the stage of asphyxia the fingers may be numb or moderately painful; during recovery from an attack the patient usually complains of either burning or of a pins and needles sensation. Except in the severest cases normal circulation can be restored and the patient then becomes symptom-free.

In the severe forms of Raynaud's disease normal circulation can only be attained at such high temperatures that the patient lives in a constant state of discomfort and partial digital asphyxia. Even in moderately warm weather such an individual may have recourse to tucking her fingers into her armpits or wearing the thickest kind of woollen gloves or fur muff. One woman said that she could get her feet comfortably warm only by putting them up before the open oven door. The result of such chronic anoxemia is terminal ulceration of the phalanges with fibrosis of the skin and subcutaneous tissue, a process which eventually ends in dry gangrene of the finger tips or a form of scleroderma.

Besides the phasic color changes and the lack of involvement of the main arteries, Raynaud's disease is characterized by its extreme symmetry. Corresponding digits become involved in the upper and lower extremities, most commonly all the toes and all the fingers except the thumbs. Rarely the ears, the tip of the nose, and in one case seen at the Massachusetts General Hospital the tongue have shown typical attacks. Raynaud (1874) also describes attacks of intermittent constriction of the retinal vessels with blurring of vision.

Excessive sweating is a common feature of the disease and in the early stages may be the patient's chief cause of complaint. The hands and feet are constantly moist and at times literally drip drops of sweat. This is particularly striking in the younger patients, who frequently comment themselves on the aggravation of this annoying condition when they become excited or emotionally upset. In the older patients or in the late stages of the disease with sclerodermatous changes hyperhidrosis is frequently absent.

impressed us that this has often followed a period of intense emotional strain, such as divorce, the death of a near relative, or financial failure. We have observed this train of events too often to feel that it can be a mere coincidence. From these observations we have come to believe that the common clinical syndrome described constitutes a prodromal form of Raynaud's malady.

Raynaud's disease is far more common in women than in men, its incidence in the female sex being approximately ten times more frequent than in the male. It generally appears between puberty and menopause, and is rarely seen in childhood or old age. A most valuable clinical study of the subject has been written by A. W. Allen in *Nelson Loose-Leaf Living Medicine*, and another by E. V. Allen and G. E. Brown (1932).

The usual case of Raynaud's disease shows no abnormality of the larger peripheral arteries, and the radial pulses, as well as the dorsalis pedis and posterior tibial arteries, can be easily palpated. Obvious vasospasm is limited to the hands and feet, with the greatest reduction of blood flow in the fingers and toes. In a warm environment the circulation may appear to be normal. Each case, however, has a critical temperature below which vasospasm sets in. Below this thermal threshold the hands and feet behave like the extremities of a cold-blooded animal. The critical temperature varies with the intensity of the disease. In a mild case it may be as low as 65, in the severe instance as high as 80 degrees. In the former the patient has no complaints in a normally heated room and gets along reasonably well out of doors with warm gloves. In this stage recovery of peripheral circulation is rapid and complete on warming, whereas in the advanced stage it takes place only slowly and incompletely even above 80 degrees For this reason the severe case cannot be comfortable even on a summer's day.

One of the characteristic features of the disease is the phasic color changes. These come on whenever the temperature falls below the critical level for the particular patient. Cyanosis, which may vary in hue from slate gray to purple, appears relatively early in the course of the disease. In advanced cases, where normal circulation is never fully restored, some degree of cyanosis persists most of the time. In the milder cases, which have not progressed to obliterative changes in the arteries, the

that of the head and trunk. Another point which they have emphasized is the surprising fact that the extremities make up 65 per cent of the surface area of the body (arms 14 per cent, hands 6 per cent; legs 38 per cent, feet 7 per cent). Loewy (1914) has estimated that, per meter of body surface, heat dissipation is greatest in the arms, next greatest in the legs,* and least in the trunk, the extremities giving off not far from 75 per cent of the total. With these data in mind, one would expect a vasomotor neurosis to affect primarily the hands and feet.

From the time of Raynaud's original description it has been recognized that the lumen of the arteries is unobstructed in the early uncomplicated stages of the disease. The site of vasospasm is not in the larger arteries, which characteristically maintain their pulsation throughout the attack, but in the digital arterioles. Landis (1930), by an ingenious method, has been able to make direct measurements of capillary blood pressure. During periods of normal circulation this amounts to 40 mm. of mercury, but during the asphyxial stage it may fall as low as 5 mm. The slowness with which capillary pressure rises when venous congestion is produced by a tourniquet during an attack, and the rapidity with which it falls on release, show that the spasm is situated on the arterial rather than on the venous side of the capillary network.

The shifts in arteriolar blood flow during the phasic color changes in Raynaud's disease have been thoroughly investigated by Lewis (1929) and Lewis and Landis (1930). In the stage of pallid asphyxia there is only intermittent leakage of blood through the intensely constricted arterioles; with lesser intensity of spasm varying degrees of acrocyanosis are manifest, depending on the reduction of the red oxygenated form of hemoglobin. The degree of dissociation of the oxygen-carrying pigment molecule depends primarily on the metabolism of the tissues and the speed of its passage through the capillary loop, also to a certain extent on the temperature. Below 60 degrees oxyhemoglobin does not dissociate easily and tissue metabolism is at a minimum, so that hands dipped in ice water may remain pink. Lewis points out that 59 degrees Fahrenheit (15 degrees Centigrade) is the most suitable temperature to bring out the

* Taken part for part, most heat is lost from the legs because of their size.

Great care must be taken in making the diagnosis of Raynaud's disease to rule out cases of primary arterial obliteration, especially in men. When the involvement is not perfectly symmetrical, and especially when the main vessels at the wrist and ankle cannot be felt, simple vasospasm should be doubted. A number of the cases reported by Raynaud himself should obviously be excluded from this category, and the literature abounds in reports of cases of thromboangiitis obliterans and arteriosclerosis masquerading under the diagnosis of Raynaud's disease. We have several times been impressed with cases of perfectly symmetrical ischemia and phasic color phenomena appearing in old age. In these instances the vasospastic phenomena have developed with unusual rapidity and increased sweating has been absent. *Arteriosclerosis can be diagnosed by x-ray evidence* of calcified vessels and the failure of full vasodilatation after diagnostic procaine block. The fact that at times arteriosclerosis may closely simulate Raynaud's disease has not been emphasized by other writers and adds considerably to the difficulty of accurate diagnosis.

Physiology. The rôle of the vasomotor system is to regulate body temperature and to maintain an adequate supply of blood to the muscles and internal organs. Its action as a thermal regulator is carried out by cutaneous vasoconstriction on exposure to cold and by vasodilatation in hot surroundings. Cutaneous vasodilatation also serves to eliminate excess body heat produced by muscular exercise or other circumstances which increase the metabolic rate. Under resting conditions 76 per cent of the body heat lost is eliminated by radiation and conduction from the skin, the remaining 24 per cent by vaporization of water from the skin and lungs. Besides cold, pain or intense emotions of fear and anger are also capable of stimulating reflex vasoconstriction, whereas such emotions as shame and embarrassment result in vasodilatation. Vasoconstriction plays the predominant rôle in pathological conditions.

Maddock and Coller (1933) have demonstrated the relative importance of the arms and legs in carrying out reflex changes in vasomotor tone. They have pointed out that the shift of blood to the surface of the body as a part of the thermo-regulatory response is not uniform in all parts of the skin, but that actually there is a much greater transfer to the extremity surface than to

that of the head and trunk. Another point which they have emphasized is the surprising fact that the extremities make up 65 per cent of the surface area of the body (arms 14 per cent, hands 6 per cent; legs 38 per cent, feet 7 per cent). Loewy (1914) has estimated that, per meter of body surface, heat dissipation is greatest in the arms, next greatest in the legs,* and least in the trunk, the extremities giving off not far from 75 per cent of the total. With these data in mind, one would expect a vasomotor neurosis to affect primarily the hands and feet.

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* Taken part for part, most heat is lost from the legs because of their size.

cyanotic hue, as at this point vasospasm is marked and oxyhemoglobin still dissociates readily into reduced hemoglobin.

Pathology. *a. Vascular Pathology.* Cassirer, quoted by Leriche and Fontaine (1932), perfused the peripheral arteries in an autopsy on a case of Raynaud's disease and showed them to be normally permeable. Recent arteriographic studies have corroborated this early observation, so that it is now generally admitted that there is no permanent narrowing of the peripheral vessels in early Raynaud's disease. However, in the stage of chronic acrocyanosis and long continued digital asphyxia very definite pathological changes set in. Spurling, Jelsma, and Rogers (1932), as well as Leriche and Fontaine (1932), have published photomicrographs of the digital vessels in such advanced cases (Fig. 40). These vessels show the organic changes of an obliterating endarteritis and are indistinguishable from those seen in long-standing Buerger's disease. With the sclerodermatous changes that are not infrequently seen in the late stages of Raynaud's disease the digital vessels are compressed by the constricting scar which invades the skin and subcutaneous tissue. In advanced sclerodactyly diagnostic procaine block fails to produce any noteworthy increase in blood flow and sympathectomy cannot be expected to produce improvement. Lewis (1938*A*) compared the digital vascular pathology of warm handed individuals with that seen in various stages of Raynaud's disease. He found that intimal thickening is the rule in the former group from the age of 50 onward, and is no more marked in the earliest stages in the latter group in patients of comparable age. He found no evidence of hyperplasia of the media in early stages of Raynaud's disease. In more advanced cases, thrombotic obstruction of the digital arteries in various stages of organization is the rule.

The capillaries in advanced Raynaud's disease commonly show a characteristic pattern which consists of a striking elongation, tortuosity, and dilatation of the loops seen in the nail bed (Fig. 41). During an attack these varicosed loops are crammed full of stagnant erythrocytes. After sympathetic denervation the dilated capillary loops contract to the normal straight, narrow type and the stagnant clumps of erythrocytes are restored to active circulation.

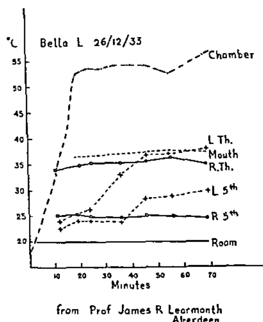




FIG 40 Postoperative vasodilatation test and photomicrographs of digital arterioles in a patient with advanced Raynaud's disease.

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courtesy of Professor James R Learmonth, Edinburgh)

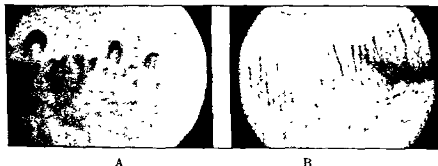


FIG 41 Dilated tortuous capillaries seen in Raynaud's disease (A) compared with those in a normal individual (B).



FIG 42 Characteristic ulcerations of finger tips in severe Raynaud's disease.

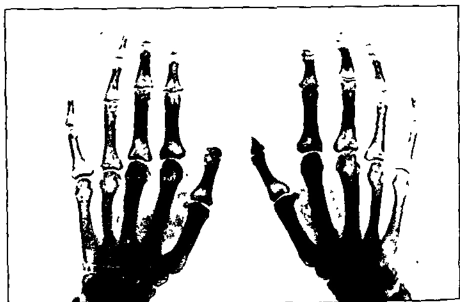


Fig. 43 Generalized decalcification and atrophy of terminal phalanges in Raynaud's disease.



Fig. 44 Terminal calcium deposits in Raynaud's disease.

b. Skin and Subcutaneous Tissue. In the early stages of Raynaud's disease there is no noticeable change in the skin. After prolonged and recurrent periods of asphyxia, however, superficial ulcers appear at the tips of the fingers, which at first tend to heal readily in warm weather. As the disease advances these areas of necrosis may extend down to the bone (Fig. 42). The growth of the nails becomes extremely sluggish and they may show extraordinary thickening and other trophic changes. Chronic paronychial infections are common (Fig. 42). In the late stages the skin of the digits and even of the entire hand or foot may become shiny and atrophic. Sclerosis occurs in the subcutaneous tissue, forming a contracting bed of scar tissue. This results in the characteristic "hide bound" picture of scleroderma. This form of scleroderma is a very different process from the diffuse type which involves the face and regions other than the extremities. In such areas, as Lewis and Landis (1931) have pointed out, evidence of a primary defect in blood flow is so slight that it cannot be regarded seriously as a cause for morbid changes in the skin.

c. Bone Pathology. Definite bone changes may develop in severe Raynaud's disease. Absorption of bone in the distal phalanges and the less common deposits of calcium in the soft tissues may be detected by x-rays (Figs. 43 and 44).

d. Nervous System Pathology. Leriche and Fontaine (1932), as well as many others, have described changes in the paravertebral sympathetic ganglia. These are characterized by narrowing of the nutrient vessels, edema of the connective tissue, lymphocytic infiltration, and degenerative changes in the ganglion cells shown by chromatolysis, vacuole formation, and abnormal pigmentation. However, Craig and Kernohan (1933), who have made a special neurohistological study of the sympathetic ganglia in 208 cases of Raynaud's disease and other allied conditions, conclude that these changes are not produced by this disease. They found identical changes in the ganglia of 40 control specimens removed from patients who had died of other conditions. The increase in pigmentation appeared to be coincident with advancing years. Similar conclusions have been reached by Dr. C. S. Kubik, who has examined the ganglia resected at the Massachusetts General Hospital.

Gagel and Watts (1932) from Foerster's clinic reported that on microscopic examination of a spinal cord in a case of Raynaud's disease they found degeneration of the sympathetic motor neuron cells in the intermediolateral cell column. If this observation is substantiated it will be one of real significance. So far as we are aware, there have been no reports of microscopic examination of the autonomic centers in the diencephalon.

A third area which may well be responsible for an increase in vasoconstrictor activity is the hypothalamus. Recent experimental evidence has shown that this is the central station for vasomotor control (Chap. IV) and a case of hypothalamic tumor with striking vasomotor manifestations has been reported by Peet and Kahn (1936).

Etiology. Raynaud (1862 and 1874) ascribed the cause of symmetrical dry gangrene of the fingers and toes without vascular obliteration to a neurosis "characterized by enormous exaggeration of the excito-motor energy of the gray parts of the spinal cord which control the vasomotor innervation." This view has been held to date by the majority of writers on the subject.

On first thought, it is remarkable that Raynaud's theory of vasomotor imbalance has gone practically unchallenged for over half a century. The first investigator to question this view was Sir Thomas Lewis (1929). As a result of his long and critical investigation of the physiology of the peripheral vessels he elaborated a theory of etiology diametrically opposed to that of Raynaud. He has concluded that vasomotor activity in Raynaud's disease is normal, but that the peripheral spasm is due to an increased susceptibility to cold on the part of the smooth muscle in the digital arterioles. An excellent summary of his views upon this matter is given in his book which deals with vascular disorders of the limbs (Lewis, 1936). Lewis has reached this conclusion from observation of the response to local cooling of the digital vessels in relatively advanced cases. He claims that when such a stimulus is applied locally to the base of a finger a typical attack of vasospasm is induced and that it is limited to this area, whereas there is no generalized reaction on the part of the sympathetic nervous system. This reaction is hard to explain on any other basis than that of a local fault. Moreover, Lewis states that it is impossible for the fingers to become completely blanched by a vasoconstrictor reflex, provided the hand

is at rest and below the level of the heart.* He has also pointed out that if the attacks of acral syncope were due to vasoconstriction, then the entire finger should blanch simultaneously instead of the attack's creeping upward from the finger-tips to the knuckles.

Two additional arguments of Lewis do not seem to us to be equally valid. In the first he assumes that procainization of the ulnar nerve at the elbow should cause complete vasomotor paralysis of the little finger. In such cases he is still able to induce well defined vasospasm on local cooling. The flaw in this argument is that in his reported cases very little vasodilatation resulted from ulnar nerve block—in these protocols the temperature of the anesthetized fifth finger rose to only 75 degrees. In several instances of severe Raynaud's disease we have failed to secure complete vasodilatation in the fifth finger until the median as well as the ulnar nerve was blocked. This may be explained by the frequent connections between the two nerves in the forearm, which may well carry some vasoconstrictor fibers. In every case of uncomplicated Raynaud's disease in which we have secured complete vasomotor paralysis, either by peripheral nerve or by paravertebral ganglion block, we have never failed to raise the digital temperature to 90 degrees and thereby rendered vasospasm from local cold quite impossible.

The second weak point in Lewis's interpretation is his argument that because he has succeeded in causing vasospasm by local cold after sympathetic ganglionectomy, the condition must be due entirely to a local fault in the digital vessels. From the work of Smithwick, Freeman, and White (1934) and Freeman, Smithwick, and White (1934) we know that after this type of operation, residual vasospasm may be accounted for on the basis of sensitivity of the denervated arteriolar muscle to adrenal secretion (see Chap. V). This phenomenon is far more striking in the hand than in the foot, because of the more complete degeneration of the postganglionic vasoconstrictor fibers after cervicothoracic ganglionectomy. In this connection, it is of interest that Lewis (1938*B*) finds preganglionic sympathectomy

*This observation of Lewis is open to question, as Simpson, Brown, and Adson (1930), who applied Lewis's tests to a series of cases of Raynaud's disease at the Mayo Clinic, stated that they observed a typical attack begin after a psychic stimulus with blanching of the fingers while the hands were at rest and below the level of the heart.

more effective than ganglionectomy in relieving attacks of vasospasm.

In addition to these objections it should be pointed out that Lewis has based his conclusions on admittedly advanced cases, which presumably had already developed obliterative changes in the digital arterioles. He has never shown residual vasospasm to local cold after lumbar ganglionectomy, an operation which is preganglionic in type. Furthermore, he has never explained the concomitant abnormal activity of the sweat glands, which is certainly a function of an overactive sympathetic nervous system, nor the characteristic predilection of the disease for hyperemotional young women.

Great credit is due to Lewis for pointing out that changes can occur in the digital arteries fairly early in Raynaud's disease. His point that total syncope of the digits indicates a local vascular fault is well taken. Photomicrographs published by Leriche and Fontaine (1932), Spurling, Jelsma, and Rogers (1932), and Lewis (1938*A*) prove that the digital vessels may be involved in an obliterating endarteritis. It is only his second point, that vasomotor tone is normal, which we may justly question. Keeping in mind all the facts which have been reviewed, we believe that the greatest weight of evidence is against Lewis's theory that the local fault is primary, and upholds Raynaud's original idea that at the onset of the disease the recurrent attacks of symmetrical vasospasm are due to an abnormal activity of the vasoconstrictor nerves. Any theory of the etiology of Raynaud's disease must be applicable to early as well as late cases, and equally to the hands and feet.

Treatment. There is no satisfactory medical treatment of Raynaud's disease. Sending the patient to a warmer climate may be sufficient for the rare individual who can afford it or can find work in the South, but even this radical change will fail to solve the problem for the severe case which fails to recover a normal circulation between attacks. Immersion of hands with normal arteries in ice-water is followed by a long period of hyperemia, but Lewis (1929) has shown that this response to supercooling fails in Raynaud's disease which has advanced to the stage of endarteritis. Various glandular extracts have been recommended, but there is no evidence to prove their efficacy. Roentgen therapy with the intention of influencing the vaso-

motor outflow from the spinal cord and dorsal ganglia has also been mentioned, but in our hands has been without the slightest effect. Allen and Smithwick (1928) reported healing ulcerations in the finger tips by fever therapy with foreign protein, but this form of treatment is too disagreeable and as a rule its benefits are too short-lived to recommend it for general use. Dinitro-phenol also produces a striking increase in peripheral blood flow and thereby promotes healing of digital ulcers, but this drug has proved to be too toxic for general therapeutic use. More recently Reynolds and Foster (1939 and 1940) studied the effect of estrin upon blood flow in the rabbit's ear and also upon cutaneous temperature and finger volume in normal male patients. A slight dilatation of minute vessels of the rabbit's ear and a small increase in finger volume without change in surface temperature was noted. Herrmann and McGrath (1940) treated 16 patients suffering from arterial deficiency with secondary vasospasm by parenteral administration of estrin. The results were not impressive. Our experience indicates that this substance may increase the range of motion and make the tissues more pliable when scleroderma is present. It has not prevented vasospasm in the early stages of the disease. The surface temperatures still fall to low levels on exposure to cold. Temporary improvement following mecholyl iontophoresis was reported by Kovacs, Saylor, and Wright (1936). Perlow (1940) noted some evidence of improved circulation after subcutaneous injections and oral administration of prostigmine. Mulinos, Shulman, and Mufson (1939) report temporary increased circulation after intravenous injections of papaverine hydrochloride preceded or followed by histamine iontophoresis.

In the management of patients with Raynaud's disease it has been our practice to make surface temperature measurements, full clinical records, and complete diagnostic tests in each case. If the disease is not severe enough to require operation the patient is re-examined each winter. It is most important to carry this out, because to combat the disease successfully operation must be performed in its relatively early stages before secondary endarteritis and sclerodermatous changes prevent a full vasodilator response.

All authorities agree that sympathectomy will benefit the milder cases. If one favors Raynaud's theory of etiology the

reason for this is obvious. Boggon (1931) and Gask and Ross (1934), who believe with Lewis (1938*B*) that the cause of Raynaud's disease is a primary fault in the digital vessels, have none the less advocated operation because the caliber of the denervated arteries is thereby increased. Thereafter spasm still occurs on local exposure to cold, but since it takes place in vessels of a larger lumen it no longer prevents an adequate circulation.

In selecting patients for operation the first essential is a correct diagnosis. Patients over 50 should be suspected of arteriosclerosis, even though they have palpable radial arteries as well as vasomotor changes and terminal ulcers of extreme symmetry. X-rays should invariably be taken in patients of this age to detect calcification of the peripheral arteries. As thromboangiitis obliterans is almost exclusively a masculine disease and Raynaud's somewhat a rarity in this sex, the former condition should be seriously considered in all male patients. When the pulsations are very faint or missing and there is any tendency to unilateral involvement, Buerger's disease is almost a certainty in a young man who is free from diabetes. We have also made it a rule to determine the basal metabolic rate, as in a few cases this has turned out to be as low as − 30 per cent. Treatment with thyroid extract has been definitely helpful in these instances.

Finally, all patients who on clinical examination appear to be suitable for sympathetic ganglionectomy should be tested by one or more of the various diagnostic procedures described in Chapter VII. In this way the patient with too advanced scleroderma or obliterative endarteritis may be spared an unnecessary and serious operation. These tests, if properly used, can be counted on to eliminate operative failures due to obliterated arteries.

Raynaud's Phenomenon. It is obvious from the foregoing discussion that there is a difference of opinion concerning the etiology of Raynaud's disease. It is also apparent that other conditions may manifest similar symptoms and color changes. It is clear that the etiology is not the same in every case exhibiting these signs and symptoms. There are several possible combinations of factors which may unite to produce such an effect. It is theoretically possible for increased vasomotor impulses to act upon normal vessels and produce these changes.

It is also possible for normal sympathetic activity to be present with vessels which are histologically normal, but hyper-reactive, and to produce nearly the same end results. Finally it is possible for pathological vessels in combination with varying degrees of sympathetic activity to produce a similar effect upon the periph-

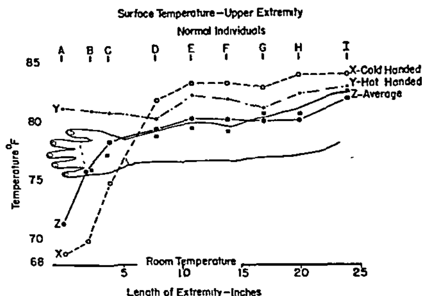


Fig 45. Surface temperature curves of normal upper extremities.

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eral circulation. Any of these combinations may result in Raynaud's phenomenon. Whether sympathectomy will help and to what extent can be predicted with considerable accuracy by the response to temporary interruption of vasoconstrictor impulses.

Interesting information can be obtained by studying the reaction of patients to their environment under identical conditions. The patient is exposed for one hour to a room temperature of 68 degrees Fahrenheit, covered only by a sheet and a thin cotton blanket from axilla to groin. Surface temperature readings are then taken at numerous standard points from the tip of a digit to the shoulder or groin as the case may be. The nature of this curve is of interest and varies in normal individuals (Fig. 45). The probable explanation for the different curves is

a variation in the amount of sympathetic activity called forth by the temperature-regulating mechanism. The significant portion of the curve is its course from the distal forearm or leg to the tip of the digits. It is of interest to note that there may be little variation in temperature levels from the distal third of the forearm or leg to the shoulder or groin from patient to patient, if the main vessel pulsations are within normal limits

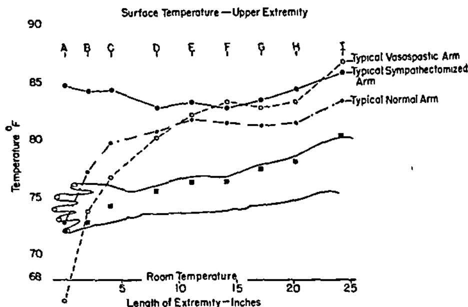


FIG 46. Surface temperature curves of an upper extremity before and after preganglionic sympathectomy for relief of vasospasm.

The typical surface temperature curve in a patient with Raynaud's phenomenon due to increased sympathetic activity is illustrated before and after sympathectomy A typical normal curve is inserted for comparison.

(Figs 46 and 47). The most marked variation in the surface temperature is noted in the more distal portions of the extremities (Figs. 45, 46, and 47).

Most patients who exhibit Raynaud's phenomenon without evidence of organic changes in the tissues have a characteristic chart in which the surface temperatures fall steadily and precipitously from the mid-forearm or leg level to the tip of the digit, the latter always being below room temperature. In other words, the curve resembles that of the cold handed normal individuals, but is set at a lower level. We interpret this as evidence of increased sympathetic activity. When the reduction of peripheral blood flow is primarily neurogenic in origin there

is also increased moisture. This results in a surface temperature which is below that of the room at the tips of the digits, and also in very low levels of skin resistance. *After nerve block, if the temperature of the tip of the finger or toe rises to 90 degrees Fahrenheit or over, it is evidence against organic vascular dis-*

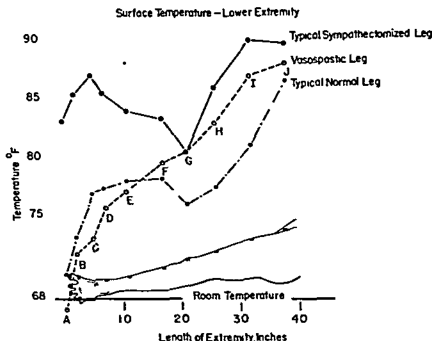


FIG. 47. Surface temperature curves of a lower extremity before and after preganglionic sympathectomy for relief of vasospasm

There is less variation between the surface temperature curves of normal and vasospastic legs than is the case with upper extremities. This is because there normally is greater sympathetic tone in the lower extremity. After complete sympathectomy, the rise in surface temperature is largely confined to the distal third of the leg (less muscular area).

ease. After sympathectomy for primary neurogenic disorders of circulation the surface temperature will be high throughout the extremity and tend to rise slightly from the mid-forearm or leg to the tips of the digits (Fig. 46).

There are also patients with Raynaud's phenomenon who have a surface temperature chart which resembles that of the normal individual. The surface temperature does not begin to fall abruptly until the mid-dorsum of the hand and foot, or base of the digits is reached. In such cases vasoconstrictor activity is not increased. The tips of the digits rarely fall to room temperature, and skin resistance levels are higher. The response

to both procaine hydrochloride and sympathectomy is less marked. Patients with known organic vascular disease such as arteriosclerosis, thromboangiitis obliterans, and some of the more advanced examples of Raynaud's phenomenon with scleroderma, ulceration, and local fault in the digital arterioles may have this type of surface temperature chart.

Methods of Denervating the Extremities. In the chapters dealing with anatomy, physiology, and the action of drugs and hormones certain fundamental principles have been discussed which have an all-important bearing upon the type of operation which should be performed and the results to be expected. These matters will be briefly summarized. The surgical technic which we prefer is described in Chapters XVII and XVIII.

To be successful an operation should be preganglionic in type and anatomically complete, and must guard against regeneration. Our experience with these matters goes back approximately fifteen years. It was a long time, however, before it became apparent that cervicothoracic ganglionectomy resulted in a postganglionic type of sympathectomy, and that lumbar ganglionectomy was preganglionic in nature. It was apparent from the start that the immediate results of operation were far superior in the leg. All agreed upon this point. We believed this could not be explained on the basis of incomplete sympathectomy, nor by the fact that vasomotor tone is greater in the lower extremity. Neither could it be explained by assuming that local fault is greater in the upper extremity, because attacks of vascular spasm recurred as early as two weeks after operation even when no local fault existed.

As these attacks occurred readily in a warm environment in response to emotion, it appeared that a humoral factor, presumably adrenine, might be concerned. Certain clinical and experimental investigations were carried out which we believe support this theory. They were reported by Freeman, Smithwick, and White (1934), Smithwick, Freeman, and White (1934), and White, Okelberry, and Whitelaw (1936). Much other corroborative evidence exists (Chap. V), but one dissenting report has recently appeared (Fatherree, Adson, and Allen, 1940). We found, among other things, that patients who had all four extremities completely denervated, and who had no local fault in any digits, were generally freed of symptoms in the feet but

not in the hands, although there was no evidence of regeneration. All these patients reacted to an intravenous injection of adrenaline in physiological concentration by a greater fall in the temperature of the fingers than of the toes. Such a case is

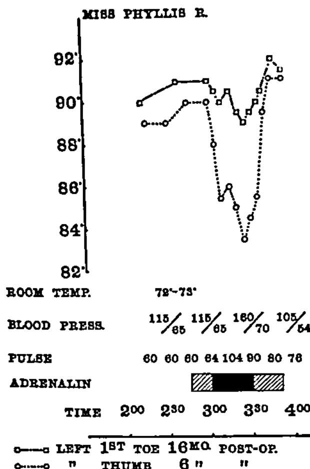


FIG. 48. Adrenaline test after pre- and postganglionic types of sympathectomy. The hands after cervicothoracic ganglionectomy show marked sensitivity to adrenaline; the feet are very slightly sensitized

presented in Figure 48. We therefore conclude that the arterioles of the hand had been rendered more sensitive to adrenine following postganglionic denervation than those of the foot after preganglionic denervation. This is consistent with well established physiological concepts (see Chap. V).

Whether this explanation is correct or incorrect, the fact remains that the immediate results of preganglionic denervation of the arm are just as satisfactory as those following lumbar

sympathectomy. Moreover, the response to adrenine in patients having both upper and lower extremities denervated by preganglionic section is the same (Fig. 49). We therefore favor preganglionic denervation both upon theoretical and practical grounds.

The leg can be easily denervated by preganglionic section. This is best performed by excision of the second and third, or

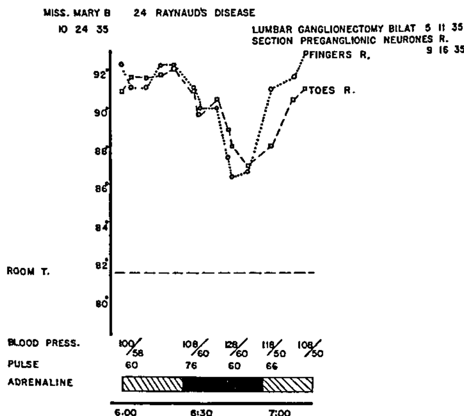
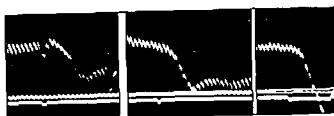
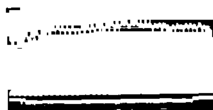


Fig. 49. Adrenaline test after preganglionic sympathectomy.

Both legs and the right arm have been denervated by preganglionic sympathectomy. One upper and one lower extremity are charted for comparison. The





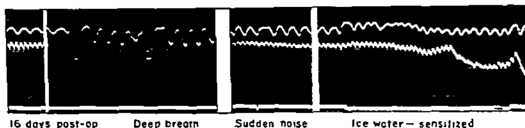


FIG. 51. Vasoconstrictor reflexes before and after sympathectomy.

Variations in blood flow were detected by the photoelectric cell, which lies beneath the … flow level on the photo- … aracteristic responses to … e are abolished Stimuli … hand in ice water The … the stimulus. Note the … which was not present at an earlier date. This presumably is a humoral effect, indicating sensitivity to adrenaline (From Smithwick, 1940C, courtesy of *Archives of Surgery*)

first, second, and third lumbar ganglia (Chap. XVIII). The arm can be completely denervated by dividing the rami of the second and third thoracic ganglia and cutting the trunk below the third ganglion (Telford, 1935; Smithwick, 1936) (Chap. XVII).* It is not necessary to divide the first thoracic white ramus because it does not carry vasomotor or sudomotor fibers of importance in man. We agree with Simmons and Sheehan (1937 and 1939) that there is no evidence of a residual sympathetic supply to the arm when denervated in this manner. Reflex sweating never occurs after this operation. Neither can a

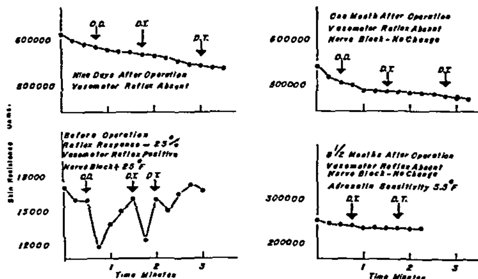


FIG. 50. Changes in skin resistance levels and abolition of reflex response after sympathectomy.

Typical record of cutaneous resistance. Before operation the level is low and variable, and a sharp fall in response to a sudden stimulus is noted. Opening the door of the room in which the patient lay or dropping a tin on the floor was [illegible] seems most likely that this fall is due to a peripheral mechanism and is not of central origin. It may, however, be an early indication of regeneration. (Modified from Smithwick, 1940C, courtesy of *Archives of Surgery*.)

* Livingston (1935) has reported an operation somewhat similar in principle which he first performed in 1931. This consists of resection of the second and third thoracic ganglia. The early results of this operation are excellent, as we ourselves had observed as far back as 1930, but we never advocated this procedure as we found that the vasoconstrictor axons invariably regenerated within 10 months (see White, 1932, Case 4, and Smithwick, 1936).

significant rise in surface temperature be demonstrated by peripheral nerve block if patients are tested two weeks or more after denervation. For reasons given on page 174, a significant rise may be detected before this period has passed, or months later if regeneration occurs (Chap. VII). We have never been able to demonstrate residual sudomotor activity by reflex skin resistance changes (Fig. 50), or persistent reflex vasomotor responses by either the photoelectric cell (Fig. 51) or finger plethysmograph. *These reflex responses have always* been present before operation. We disagree with Kuntz, Alexander, and Furcolo (1938), who infer that the first thoracic segment carries important sympathetic fibers to the upper extremity in man because they can be demonstrated in cats. Recent investigations by Sheehan and Marrazzi (1941) also indicate that in monkeys the first thoracic segment does not carry any sympathetic fibers to the upper extremity which can be detected by as sensitive a recording mechanism as the cathode ray oscillograph.

Regeneration has always been a problem in the upper extremity. Even after resection of the inferior cervical, first and second thoracic ganglia regeneration may eventually take place to a significant degree. This has also been the case after the various forms of preganglionic sympathectomy, following which regeneration may appear earlier and be more complete (Fig. 52). This has necessitated several changes in technic: first ramisectomy, then extraspinal root section, then intraspinal root section, and finally protection of the decentralized second and third ganglia by enclosing them in a fine silk cylinder (Smithwick, 1940*A* and *B*) (Chap. XVII, Figs. 71 and 72). From the clinical point of view the late results have far surpassed those obtained by the older cervicothoracic (postganglionic) type of sympathectomy, but after the earlier modifications of this operation objective evidence of regeneration was frequently discovered. At present many cases show no signs of regeneration three to five years after operation. We hope that silk will result in the formation of an impenetrable capsule of scar tissue about the decentralized ganglia and thereby prevent subsequent ingrowth of neurofibrils, as Page (1940, unpublished data) has observed after silk has been wrapped about the kidney. The variation in the tendency to regenerate which one notices in different patients after similar or identical operations is most

likely related to variations in the origin of the sympathetic supply from the cord. Thus when the vasconstrictor outflow from the second and third thoracic segments is most important, regeneration can be expected to occur more rapidly than when

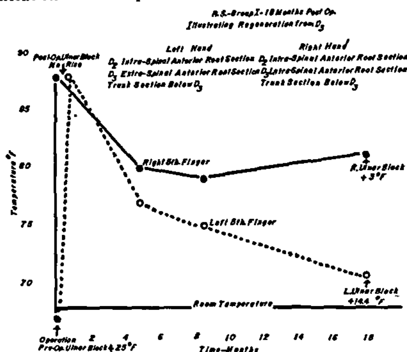


Fig. 52. Regeneration following sympathetic denervation of upper extremity. The late results of different operations upon the surface temperature of the fifth finger tips of the two extremities of the same patient are contrasted. The patient was exposed to a cool environment at various intervals after operation. If it is safe to assume that the nerve supply to the arms is similar in the same

Surgery)

most of the fibers arise in midthoracic levels, as the distance which they must travel to restore continuity is shorter. This matter has been discussed in detail by Smithwick (1940B). Regeneration occasionally follows lumbar sympathectomy if the resection has not been extensive enough (Fig. 53). It is important that the divided distal end of the lumbar trunk be ligated and displaced as far as possible from the source of re-

generating fibers. These may come from the first and second, rarely from the third lumbar nerves. Atlas (1940) found evidence of a white ramus connecting the second lumbar ganglion and the third lumbar nerve in only 1 of 31 dissections. In the

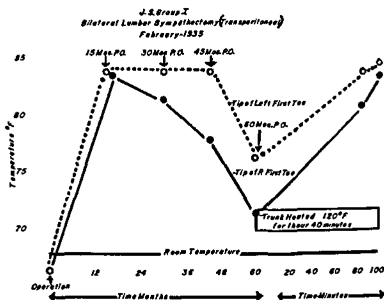


FIG. 53. Regeneration following sympathetic denervation of lower extremity. Regeneration of sympathetic pathways to the foot occurs more frequently after transperitoneal operation because in some cases it is difficult to obtain satisfactory exposure Consequently inadequate resection results In this case of Raynaud's disease the surface temperature of the tips of both great toes was measured periodically after exposure to a room temperature of 68 degrees [illegible] was apparent on the right side in 30 [illegible] the Regeneration occurred to a lesser [illegible]

courtesy of *Surgery*)

other 30 there was only a single connection between these structures.

Results. From January, 1935, to January, 1941, 158 upper extremities have been denervated in 97 patients. There have been no deaths. The results of operations for vasospastic disorders are presented in Table III. They depend principally upon the degree of local fault which is superimposed on the neurogenic spasm of the vessels and on the amount of regeneration after sympathectomy. This was most apparent after ramisectomy. From February, 1940, to January, 1941, 20 upper extremities in 15 patients have been denervated by ramisectomy, extra-

TABLE III. PRIMARY VASOMOTOR DISORDERS: UPPER EXTREMITIES DENERVATED BY PREGANGLIONIC SYMPATHECTOMY

	No. of Extremities	*Clinical Result*		
		Good	Improved	Unimproved
Group I . . .	33	28 (Excellent)	3	2
Group II . . .	34	25 (Very good)	8	1
Group III . . .	26	12	12	2
	93	65	23	5

This table includes all cases with either Raynaud's disease or Raynaud's phenomenon. They are divided into three groups according to the degree of local fault. This was absent in Group I. Obvious soft tissue changes were present in Group II, and consisted of ulceration, gangrene, or varying degrees of scleroderma without x-ray changes In Group III, calcification of soft tissues or atrophy of terminal phalanges was evident from x-ray studies. A preganglionic type of sympathectomy was performed in all cases, but three modifications were used: ramisectomy, extraspinal root section, and intraspinal root section. These changes were made primarily to prevent regeneration. The best results followed intraspinal root section. Cases in which the decentralized second and third ganglia were enclosed in a silk cylinder are not included. See Chapter XVII for further discussion of surgical technic. The unimproved results in Groups I and II were due to incomplete sympathect[illegible] [illegible] changes which prevented vasodilatation

TABLE IV. MISCELLANEOUS DISORDERS: UPPER EXTREMITIES DENERVATED BY PREGANGLIONIC SYMPATHECTOMY

Diagnosis	*No. of Cases*	*No. of Extremities*	*Clinical Result*		
			Very Good	Improved	Unimproved
Rheumatoid arthritis with vasomotor spasm . . .	5	7	3	2	2
Causalgia	4	4	2	2	—
Hypertension: marked vascular spasm after splanchnic resection	1	2	2	—	—
Frostbite with gangrene . .	1	1	—	1	—
Thrombosis of brachial artery:					
(a) Without abnormality of ribs	4	5	3	2	—
(b) With abnormality of ribs	2	2	2	—	—
Arteriosclerosis with gangrene or ulceration	6	10	4	5	1
Thromboangiitis obliterans with gangrene or ulceration	6	7	3	4	—
Hyperhidrosis	5	9	9	—	—
Totals	34	47	28	16	3

spinal or intraspinal root section, the decentralized ganglia being covered by a silk cylinder in every case. It is too early to evaluate this method, but the results thus far are encouraging. There has been no untoward reaction from the use of silk, and no evidence of regeneration. Table IV contains a miscellaneous group of conditions in which sympathectomy has been found useful.

From May, 1936, to January, 1941, 146 lower extremities in 99 patients have been denervated by the extraperitoneal route. One death resulted from a pulmonary embolism. The results of these operations in 61 patients who have been followed for over a year are given in Table V.

TABLE V LOWER EXTREMITIES DENERVATED BY PREGANGLIONIC SYMPATHECTOMY

Diagnosis	*No of Cases*	*No. of Extremities*	*Clinical Result* Very Good	Improved	Unimproved
A. VASOMOTOR DISORDERS					
Raynaud's disease	9	18	18	—	—
Vascular spasm and old poliomyelitis	5	6	6	—	—
Vascular spasm and degenerative spinal cord lesion	1	1	—	1	—
Vascular spasm and spina bifida	1	1	—	1	—
Vascular spasm and chronic ulceration associated with varicose veins or recurrent lymphangitis	3	4	2	1	1
Total	19	30	26	3	1
B. OBLITERATIVE VASCULAR DISEASE AND OTHER DISORDERS					
Thromboangiitis obliterans	30	52	22	27	3
Arteriosclerosis with gangrene	4	6	2	4	—
Frostbite with gangrene	2	3	—	2	1
Causalgia	2	2	—	1	1
Hypertension — gangrene of foot following splanchnicectomy	1	1	1	—	—
Gunshot wound femoral artery	1	1	—	—	1
Popliteal aneurysm	1	2	—	2	—
Hyperhidrosis	1	2	2	—	—
Total	42	69	27	36	6

The patients reported in this table are those in which the extraperitoneal approach was used. Previous to May, 1936, we denervated the lower extremities by transperitoneal sympathectomy. The technic for both procedures and their relative merits are discussed in Chapter XVIII.

II. Other Forms of Peripheral Vascular Disease Which Can Be Treated by Sympathectomy

Vasospasm Associated with Lesions in the Spinal Cord. Numerous victims of anterior poliomyelitis and occasional cases of pyramidal tract disease complain of coldness and discoloration in their paralyzed legs. These manifestations are usually of vasospastic origin and, if they respond suitably to diagnostic procaine block, can be greatly improved by sympathectomy. At one time we felt that the results of lumbar sympathectomy after infantile paralysis when associated with extensive loss of muscular activity were not wholly satisfactory (White, 1931). Experiences of recent years, however, indicate that the inferior results were related to inadequate (transperitoneal) denervation. Since employing the extraperitoneal approach and removing the first, as well as the second and third lumbar ganglia, the results have been satisfactory (Table V).

Thromboangiitis Obliterans and Arteriosclerosis. Numerous individuals have organic vascular disease in addition to an abnormal degree of vasospasm. This may be confined largely to the digits, or may be very diffuse and involve the whole extremity. Surgical intervention upon the sympathetic nervous system may be very helpful in the management of some of these patients (Smithwick, 1940*C*). Arteriosclerosis with diabetes is almost never associated with a significant degree of vasospasm. On the other hand, thromboangiitis obliterans frequently has a large element of arterial spasm. In its early stages it may be impossible to distinguish this condition from a primary vasomotor disorder. When preliminary tests indicate a favorable response sympathectomy has been found helpful in the presence of known organic disease. We have employed sympathectomy in many cases of thromboangiitis obliterans, generally in combination with other forms of treatment such as minor amputation of digits and crushing of peripheral nerves (Smithwick and White, 1930 and 1935). The results are given in Tables VI, VII, and VIII. In general, we are impressed by the additional benefit which has followed sympathectomy in many of these patients. When, however, all main vessel pulsations including that in the femoral artery are lost, sympathectomy is usually of no avail, especially when ulceration, infection, or gangrene are present.

The indications for peripheral nerve crushing are discussed in Chapter XXI.

Peripheral arteriosclerosis may at times be associated with enough vasospasm to justify interruption of sympathetic pathways. Several such cases are reported in Tables IV and V. This may apply to both upper and lower extremities. Besides improvement in the circulation to the skin and subcutaneous tissue, muscular circulation may also occasionally benefit, as judged by improvement in or disappearance of intermittent claudication. This also applies to some patients with thromboangiitis obliterans. Freeman (1941, personal communication) has recently performed lumbar sympathectomy in a small series of

TABLE VI THROMBOANGIITIS OBLITERANS: RESULTS OF VARIOUS FORMS OF TREATMENT AS JUDGED BY THE INCIDENCE OF MAJOR AMPUTATIONS IN CONSECUTIVE CASES

Form of Treatment	*No of Extremities*	*Successful Minor Amputations*	*Major Amputations*	*Percentage Major Amputations*
Non-surgical: rest, vascular exercises, cessation smoking, etc.	31	7	23	74 2
As above plus crushing peripheral nerves	26	14	8	30 8
As above plus sympathectomy	20	14	3	15 0

The addition of nerve crushing and sympathectomy seems to have resulted in a decrease in the percentage of major amputations, and an increase in the percentage of successful minor amputations.

TABLE VII. THROMBOANGIITIS OBLITERANS: RELATION BETWEEN MAIN VESSEL PULSATION AND RESULT OF SURGICAL TREATMENT IN CONSECUTIVE CASES

Pulsation Popliteal Artery	*Form of Treatment*	*No. Extremities*	*Percentage Major Amputations*
Present	Crushing peripheral nerves	16	25
Present	Crushing peripheral nerves followed by sympathectomy	27	0
Absent	Crushing peripheral nerves	17	47.1
Absent	Crushing peripheral nerves followed by sympathectomy	23	13 0

Sympathectomy in addition to peripheral nerve crushing seems to have improved the results both in the presence and absence of popliteal pulsation.

TABLE VIII. THROMBOANGIITIS OBLITERANS: FIFTY CONSECUTIVE CASES TREATED BY SYMPATHECTOMY, ARRANGED ACCORDING TO MAIN VESSEL PULSATION *

Pulsation of Main Vessels	*No of Extremities*	*Peripheral Nerves Crushed*	*Minor Amputation Performed*	*Major Amputation Necessary*
Present in all	8	0	0	0
Absent in either dorsalis pedis or posterior tibial or both. Present in popliteal	19	5	3	0
Absent in popliteal. Present in femoral	21	14	11	2
Absent in femoral	2	1	0	1
Total	50	20	14	3 (6%)

When all forms of medical and surgical treatment are combined and utilized as indicated, the incidence of major amputations is reduced. The incidence of major amputations is highest when extensive main vessel obliteration is present.

* Careful hygiene, vascular exercises, and cessation of smoking were also insisted upon.

patients for relief of intermittent claudication after first demonstrating that this symptom could be improved or was abolished by paravertebral block with procaine hydrochloride. In dealing with patients having known organic disease one must demonstrate by one method or another (Chap. VII) that the circulation can be improved before recommending sympathectomy. We recognize, however, that there is a small group in which preliminary tests do not indicate that operation will be effective, yet experience has shown it to be surprisingly worth while in some instances. No satisfactory method of study has been devised for this group. Only the most experienced should proceed with surgical intervention upon sympathetic pathways under these circumstances.

Chronic Ulceration of the Extremities. *Occasionally chronic* indolent ulceration in the lower third of the leg may follow deep thrombophlebitis, varicose veins, or recurrent bouts of cellulitis with abscess formation and subsequent fibrosis. When such ulcers fail to respond to ordinary methods of treatment, study may reveal a large element of vasospasm associated with the organic changes. This probably is best explained by assuming that these particular individuals have always had more than the average amount of peripheral sympathetic activity. In some cases, however, the latter may be secondary to the local lesion, particularly if pain is a significant factor. When preliminary tests are

favorable, improvement has followed sympathectomy. Craig and Brown (1930) reported a successful case treated in this manner.

Frostbite may result in varying degrees of chronic vascular disease of the digits and distal portions of the extremities. When this is associated with excessive vasoconstriction, circulatory difficulties ensue. Some of these patients may also benefit from sympathectomy.

We have found sympathectomy to be helpful in the management of a few cases of thrombosis of the brachial artery with chronically impaired circulation. At times this condition is associated with a cervical rib or an anomalous first rib, although there may be no such abnormality. Aside from pain due to compression of the brachial plexus, gangrene of the digits and intermittent claudication may also be present. Lewis (1936) feels that these complications are due to occlusion of the arterial tree by emboli. This phenomenon is usually associated with lowered surface temperature, and the main vessel oscillations may be reduced or absent. While section of the scalenus anticus muscle combined with resection of the rib back to the transverse process usually relieves the brachial neuritis, it is not likely to improve the circulation. In several such cases gratifying improvement of the collateral circulation with marked elevation of surface temperature, healing of ulceration, and relief of intermittent claudication has followed preganglionic section, even when oscillations have not been significantly changed. As a rule, we have employed the anterior approach (Telford, 1935) under these circumstances (Table IV).

Acute Occlusion of Major Peripheral Vessels. Following sudden occlusion of major peripheral arteries the danger of gangrene is great. The lower extremity is more vulnerable than the upper, as the collateral circulation is inferior. In addition to mechanical interruption of main vessel flow by one cause or another, spasm of the entire vascular bed distal to the lesion may follow. If the collateral circulation fails to carry enough blood to the tissues, diffuse thrombosis will follow and gangrene will develop. Animal experiments of Stricker and Orban (1930), Reichert (1932), Oughterson, Harvey, and Richter (1932*A* and *B*), and Theis (1933) show that these changes can be minimized

or entirely eliminated by interruption of vasoconstrictor impulses.

Gage and Ochsner (1940) recommend early interruption of the sympathetic supply to the extremity in question by paravertebral alcohol injection. They report excellent clinical results in 10 cases in which this procedure was utilized before ligation of major peripheral arteries. Their results are most impressive and indicate that the common iliac or common femoral arteries can be ligated successfully in this way without evidence of ischemia or deficiency of the peripheral circulation. Equally impressive were the results in 4 cases of embolic occlusion of the common femoral artery. Also, several peripheral aneurysms were treated by chemical sympathectomy as a preliminary to ligation or endo-aneurysmorrhaphy. Veal (1940) favors surgical interruption of appropriate portions of the lumbar and thoracic sympathetic trunks when a more lasting effect is desirable, and reports 3 excellent results when ligation or endo-aneurysmorrhaphy was combined with lumbar or thoracic sympathectomy.

It would appear that prompt elimination of vasospasm by paravertebral alcohol injection, or when possible by sympathectomy, should go far toward reducing the incidence of gangrene in cases of laceration, embolic occlusion, or ligation of major peripheral arteries. Other adjuncts such as heparin should also be employed. Murray (1940) has described how effectively this substance prevents thrombosis. It should prove invaluable in the management of various types of vascular lesions. Intermittent venous occlusion (Collens and Wilensky, 1939), passive vascular exercises (Landis and Gibbon, 1933; Herrmann and Reid, 1933; Herrmann, 1936), and the oscillating bed (Sanders, 1936) may also be used to hasten the development of collateral circulation.

An appreciation of the rôle of vasoconstrictor spasm in thrombophlebitis was first aroused by the report of Leriche and Kunlin (1934). DeBakey, Burch, and Ochsner (1939) have presented experimental evidence to show that reflex spasm of peripheral arteries and veins follows chemical irritation of a venous segment. The diminution of peripheral pulsations and rise of venous pressure which resulted could be prevented or abolished

by interruption of sympathetic pathways. The importance of this mechanism in the production of the clinical manifestations of deep thrombophlebitis has been emphasized by Ochsner and DeBakey (1939, 1940*A* and *B*). Excellent results followed early and repeated procaine hydrochloride block of the lumbar ganglia in 20 cases. These include prompt relief of pain, reduction of swelling, and improvement in circulation. Some cases have been followed for one year. No postphlebitic sequelae such as swelling, superficial varices, or ulceration have been observed. The rôle of vasospasm in acute lesions involving major peripheral vessels has been summarized by Smithwick (1941).

Erythromelalgia. The condition known as erythromelalgia consists of redness and burning pain of the extremities. It may become totally incapacitating and render the patient incapable of tolerating the lightest pressure or covering of the feet. The attacks are brought on by heat, exercise, and the dependent position of the extremity. Arterial pulsations are present and the vessels to the feet greatly dilated. Erythromelalgia is in many respects the antithesis of Raynaud's disease. Weir Mitchell (1878), who first described it, considered the lesion to be a rare vasomotor neurosis of the extremities. It is known that vasodilatation in response to heating is mediated by the thoracolumbar sympathetic neurons and that the vessels of a sympathectomized extremity are incapable of dilating, as well as constricting (see p. 83). From a knowledge of these facts Telford and Simmons (1940) have submitted 3 patients to lumbar ganglionectomy. In all of these pain was abolished and circulation in the feet returned to normal. The results in their first case have been followed for four years. While we have had no personal experience with this condition, the reported results are striking and the treatment appears to be most logical.

III. Hyperhidrosis of Nervous Origin

List and Peet (1938*A*, *B*, and *C*) in their excellent articles on the activity of the sweat glands have shown that these structures respond both to thermal and to psychic stimuli. While sweating to eliminate heat is a generalized process and is rarely a cause for complaint, hyperhidrosis of nervous origin may become extremely annoying and even incapacitating. The latter variety is usually limited to the palmar and plantar surfaces and

the fingers and toes. Above the wrists and ankles perspiration is normal. The clamminess of hands and feet may be really disabling. Beads of perspiration may form on the finger-tips and wet everything the patient handles. Shaking hands may become most embarrassing; as one of our patients, a lawyer complained: "The law is a handshaking profession and I can't do it!" Another patient, a medical student, could not assist at operations because the sweat ran over the tops of his rubber gloves. The feet commonly perspire to a similar extent, so that the lower part of the sock or stocking is dripping wet. The feet of one of Telford's (1938) patients sweated so excessively that the man, a letter-carrier, was forced to take off his boots and empty them of water several times a day. Excellent photographs of the excessive degree of sweating which may be seen in this condition are to be found in an article by Adson, Craig, and Brown (1935).

This type of hyperhidrosis is usually accompanied by some degree of vasospasm, so that the sweaty extremities are frequently cold and at times cyanotic. As patients with Raynaud's disease often have extremely moist, as well as cold, extremities, the two conditions seem to shade imperceptibly one into the other. Unlike Raynaud's disease, hyperhidrosis is frequently seen in men, but both diseases are likely to occur in young and emotionally unstable individuals.

Etiology. No specific etiologic factor is known for this form of hyperhidrosis, but it is brought about by hyperactivity of the sympathetic nervous system and is exaggerated by nervousness. Just as generalized sweating is frequently seen in high strung thoroughbred horses in the paddock before a race, in human beings the more localized variety of nervous sweating can be brought out by any difficult mental problem or embarrassing situation. When the normal individual is terrified and breaks out in a "cold sweat," it is the hands and feet that are most strikingly involved. As a result of recent investigations on the rôle of the premotor cortex and the autonomic centers in the hypothalamus, it is now known that all forms of visceral activity may be influenced by the psychic state of the individual (Fulton, 1936). Darrow (1937) has emphasized the point that the secretory function of the palms is to provide an adhesive surface and to improve the grip, thereby providing "a teleologic ra-

tionalization of the frequently observed association of palmar sweating with certain aspects of adaptive behavior." Actually palmar sweating represents one of the homeostatic mechanisms of preparation for activity. It disappears in sleep when autonomic activity is reduced and differs from heat sweating, in which the palmar surfaces are usually dry. As Darrow has pointed out, the condition of the hands and feet may become really disabling in persons in whom "anticipatory preparation or apprehension has become exaggerated into chronic anxiety."

Treatment. In the treatment of severe hyperhidrosis medical measures have been unsatisfactory. Application of antisudorific preparations, such as 5 per cent formalin, bring about some local reduction in sweating, but at the price of maceration and irritation of the skin. Radiation of the skin may cause some atrophy of the glands, but it must be pushed to the point of risking a chronic dermatitis. As spontaneous activity of the sweat glands is mediated by the sympathetic nerves, it ceases entirely when these pathways are interrupted. Charts showing the areas of anhidrosis after various operations on the sympathetic nervous system have been published by Roth (1937).

Sympathectomy was first carried out to reduce hyperhidrosis by Kotzareff (1920) in 1919. In this operation the resection included only the cervical ganglia, but the excessive sweating appears to have stopped. The anatomical and surgical aspects of this condition were thoroughly explored by Braeucker (1928) and by Hesse (1930). The former stated that the sympathetic sudomotor axons to the hand run over the rami communicantes of the two lowest cervical and the first thoracic ganglia. Hesse (1930) and his colleague Juzelevskij, however, found that some additional lower fibers leave the second thoracic ganglion, and this has been confirmed by Kuntz (1927). According to Langley (1892) and Braeucker (1928) these fibers leave the spinal cord in the motor roots from the fourth to the ninth thoracic segments. Recent observations of Kuntz, Alexander, and Furcolo (1938) demonstrate that there are higher fibers which emerge over the second and third intercostal nerves, and that a few fibers to the sweat glands in the cat's paw run in the first thoracic root. Clinical experience has shown that sudomotor axons leave the cord as high as in the second and third thoracic roots, but the results of the operation reported below make it extremely un-

likely that any originate above the second thoracic nerve in man. As is the case with the vasoconstrictor fibers, all these preganglionic axons, after reaching the paravertebral sympathetic trunk, run upward to the two lowest cervical and upper two thoracic ganglia, where they establish synapses with postganglionic neuron cells whose axons are distributed to the cords of the brachial plexus over the gray rami communicantes (Fig. 28). The nerve supply to the sweat glands of the foot leaves the cord over the lowest thoracic and upper two lumbar nerves, and is distributed to the roots of the sciatic nerve from the fourth lumbar to third sacral ganglia.

Neurosurgical relief of extreme hyperhidrosis of the extremities has been called to the attention of the medical profession through the reports of Braeucker (1928), Pieri (1932), Leriche and Frieh (1934), and Roberts (1934), and the more recent article by Adson, Craig, and Brown (1935) in this country. In the Massachusetts General Hospital the operation was first performed in 1932. Standardized procedures are now available to sever the sympathetic fibers running to the upper and lower extremities. As the vasomotor and pilomotor are mixed with the sudomotor fibers, the operation diminishes vasoconstrictor tone in addition to causing a total paralysis of sweating and of pilomotor activity. In the case of the lower extremities resection of the second and third lumbar ganglia can be counted on to stop all sweating below the knees,* as well as to produce a lasting vasodilatation.

In the case of the arm the sympathetic pathway may be interrupted in its postganglionic portion by cervicothoracic ganglionectomy as proposed by Adson (1934). This results in a Horner's sign which is somewhat disfiguring, particularly when the operation is done only on one side. Cervicothoracic ganglionectomy results in clinically satisfactory paralysis of the sweat glands (although minor degrees of regeneration are not uncommon, p. 204), and its action is not affected by the sensitization phenomenon as it is in the case of Raynaud's disease (p. 119). Unlike the blood vessels, which become sensitized to adrenine and sympathin, the sweat glands are cholinergic (see Chap. V).

* Except for a narrow zone along the inner calf and medial malleolus, which is innervated by the saphenous nerve. This is a branch of the anterior femoral and, as such, derives some of its sympathetic connections from the first lumbar ganglion.

When denervated they continue to react to acetylcholine (List and Peet, 1938*C*), but this compound is too quickly destroyed in the circulating blood to be of any clinical significance. Nevertheless we believe preganglionic sympathectomy to be a better operation, not only because it avoids the oculopupillary paralysis, but also because these patients usually have cold as well as sweaty hands and should be given the added benefit of the most effective vasodilatation.

The operation must usually be carried out bilaterally. As is the case with Raynaud's disease, it is safest to perform these operations in stages. The second operation can usually be performed four days to a week after the first, so that the total period of hospitalization is generally under a fortnight when both arms are denervated, and less than three weeks if both lumbar chains are resected.

Hyperhidrosis in the hands was relieved in one case by paravertebral infiltration of alcohol around the upper three thoracic ganglia, with only a single night's hospitalization and without any interruption of the patient's employment. Nevertheless it is our belief that with rare exceptions surgical denervation is the better procedure, as its action is certain and the operative risk is almost nil in this group of young and otherwise healthy individuals. After alcohol block there is considerable risk of incomplete results and some risk of producing troublesome intercostal neuritis.

The consistently satisfactory results of surgical intervention in hyperhidrosis are shown by the fact that in 5 cases treated by surgical denervation and 1 case by paravertebral alcohol injection the condition was relieved in all.* In the first patient, treated by resection of the first and second thoracic ganglia, there was a partial recurrence after 8 years. The same is true of the patient treated by chemical denervation, but the hands of these individuals sweat no more than normal extremities, and the patients themselves are perfectly satisfied with the result. The other 4 patients have had dry extremities since their operations (Table IV).

* [illegible]

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CHAPTER IX

EXTREMITIES: BONES, JOINTS, AND PAIN

I. Effect of Sympathectomy on Bone Growth

IT is a common clinical observation in children that tuberculosis in a joint may cause increased growth of bone at the neighboring epiphyses and abnormal lengthening of the extremity. This is due to local hyperemia. On the other hand, the more diffuse hyperemia of sympathectomy does not cause an increased growth either of bone or soft tissue, at least in normal young animals. Cannon (1932) has demonstrated this by observing the growth of kittens after total extirpation of the paravertebral sympathetic ganglia from one side of the body. Similar observations following lumbar ganglionectomy have been recorded by Simon (1930) in young rabbits, and by Bisgard (1931) in kid goats.

These negative results in normal animals do not necessarily rule out the possibility of accelerating growth activity in epiphyses whose blood supply is pathologically reduced. Favorable results from lumbar ganglionectomy have been reported by Harris (1930) and by Harris and McDonald (1936) in children with residual paralysis after anterior poliomyelitis. These young cripples frequently develop a striking impairment of circulation in their paralyzed legs and a secondary retardation of growth. In their series of 46 ganglionectomies hyperemia was maintained in 32, and in 26 of these the rate of growth increased on the operated side. This increased growth resulted in reducing the disparity in length up to an inch in the first year. In selecting these cases it is important that the subject should be young, so that a long period of growth remains; also that the extent of the paralysis should not be excessive, because muscular activity is a

necessary stimulus to growth. Wilson and Thompson (1939) have recently reviewed the different methods of leg lengthening. They conclude that when performed on a child under nine lumbar ganglionectomy is capable of producing a maximum of one inch increased growth in the shortened extremity. This method of equalizing leg length is less effective than orthopedic measures for lengthening the bones of the leg directly or shortening those of the normal leg. On the other hand, improvement in circulation in the cold, cyanotic, and at times ulcerated legs which are seen in these young cripples may be a strong argument in favor of sympathectomy. Experience with this operation has taught that when sufficient motor function remains so that the leg can be used in walking, a worthwhile permanent increase in circulation can be counted on (White, 1931). This fortunately is the type of leg in which the prevention of shortening is of the greatest value. In the completely paralyzed extremity less lasting improvement of circulation can be obtained, and sympathectomy is definitely contraindicated. Our personal experience with this procedure has been very limited, but the following protocol illustrates the type of case suitable for sympathectomy and the result that may be obtained.

Paul P., 9, M G.H. #3546. This boy was first seen in the out-patient department as a baby of 2 because he did not move his left leg. The tentative diagnosis was anterior poliomyelitis, and he was followed in the orthopedic clinic. In 1939 he was referred to the neurosurgical service because of progressive shortening of his partially paralyzed leg and coldness of the foot.

The boy had a patchy paralysis of moderate degree involving the muscles of his left lower leg, with toe drop With the aid of a caliper brace he walked well, but the left leg was 1¼ inches shorter than the right. In addition his left foot was distinctly colder and bluer than the right, but it showed satisfactory vasodilatation on diagnostic procaine block.

1/17/40: Left lumbar ganglionectomy (L_1–L_3).

The boy made an uneventful recovery and has maintained the striking vasodilatation of his foot and lower leg. Recent measurements made by teleoroentgenogram show that in the sixteen months since operation his left leg has had an accelerated rate of growth. Whereas it was formerly 1¼ inches shorter than the right leg, it is now only ⅝ of an inch shorter.

A technical point about the operation is worthy of emphasis. This concerns the ganglia which must be removed. In the or-

dinary case of Raynaud's disease, where the poor circulation is limited to the foot, resection of the second and third lumbar ganglia is sufficient. But in this condition, where it is most desirable to increase circulation as high as the upper tibial and lower femoral epiphyses, it is important to carry the resection as high as the first lumbar ganglion. Fontaine, Houot, and dos Santos' (1937) studies on circulation and also the determinations of postoperative sweating by Smithwick (unpublished data) show clearly that it is necessary to remove the upper lumbar ganglion in order to secure a complete sympathetic paralysis as high as the mid-thigh.

II. Effect of Sympathectomy on the Healing of Fractures

Investigation of the effect of sympathectomy on the healing of fractures in animals does not, on the whole, favor acceleration of the reparative process (Pearse and Morton, 1931; Key and Moore, 1933; and Zollinger, 1933). These authors include a review of earlier work in which an opposite conclusion had been reached.

Periarterial sympathectomy has been frequently advocated by European surgeons to stimulate bone repair and the healing of fractures. Among these may be mentioned Kappis (1923), Rubaschow (1925), Fontaine (1926), and Stropeni (1926). It is to be noted that, with the exception of Fontaine, no author reported more than 3 cases. In the latter's experience, 4 patients appear to have been definitely benefited, while in a corresponding number there was no apparent improvement. In this country Colp and Mage (1931) report clinical healing in 8 of 10 cases of ununited fracture of the lower extremity within an average period of three weeks after this operation. The treatment of ununited fractures by periarterial sympathectomy seems to us utterly illogical. In the first place it is far more reasonable to treat the fracture itself by freshening the opposed surfaces and adding available calcium in the form of bone chips or a bone graft. This operation will result in a general, as well as a local, hyperemia at least as great as that which could be produced by periarterial sympathectomy (cf. p. 232). In the second place, even in the presence of an active hyperemia, it is doubtful whether circulation can be effectively increased at the point where it is most needed—at the line of fracture. As Meyerding

has pointed out in his discussion of Colp and Mage's paper, injection of the arteries in specimens of old ununited fracture *shows that few large vessels penetrate through the dense layer* of scar tissue which surrounds the fracture.

III. Rheumatoid Arthritis (Atrophic, Proliferative, or Chronic Arthritis)

The function of the sympathetic nervous system in normal and pathological joints is not well known. It has not been possible to measure how much control these nerves exert over the circulatory activity of the synovial membrane and the consequent changes in the rate of diffusion of synovial fluid. The effect of sympathectomy on arthritic pain is variable. From the best available evidence *articular sensation is mediated entirely* through the peripheral spinal nerves.

In the typical case of Raynaud's disease, even when it progresses to the sclerodermatous stage, changes in the articulations are rare. On the other hand, it is not uncommon for a patient with rheumatoid arthritis in the peripheral joints to show strikingly cold, sweaty, cyanotic extremities. It is difficult to tell in this condition which is the primary process. Pollock (1930) cited John Hunter's early description of the disproportionate weakness and atrophy of the muscles which may follow injuries to joints. Vulpian believed that numerous types of peripheral lesions such as frostbite, burns, and deep wounds, were *at times* a cause of trophic disturbances in the skin and impairment of the circulation. Pollock, in summarizing the experiences of Babinski and Froment with injuries of this type in the first World War, agreed with them that the vasomotor manifestations common to all these conditions arise from a reflex disturbance of the sympathetic centers.

The effect of cervicothoracic and lumbar ganglionectomy has been tested on a considerable number of patients with rheumatoid arthritis and associated vasospasm. Rowntree and Adson (1927) first advocated this procedure and claimed to have achieved freedom *from pain with arrest or even retrogression of the disease.* In a report of surgical results in a series of young patients with the periarticular type of arthritis, predominantly confined to the lower arm and leg, and in whom the circulatory defect responded well to release from control of the vasoconstrictor nerves, Adson

(1933) stated that 70 per cent gave a favorable response. But with the exception of Flothow (1930, 5 cases), Leriche and Jung (1933, 2 cases), and Young (1936, 7 cases), few surgeons have been able to obtain satisfactory results. In addition, it is highly significant that no further follow-up reports have emanated from the Mayo Clinic, after their early enthusiastic papers.

At the Massachusetts General Hospital 5 patients, who have been studied in the arthritic clinic by Dr. Walter Bauer, have been operated upon. The results in these cases, which fulfilled the requirements laid down by Rowntree, Adson, and Hench (1930), have been distinctly disappointing. The patients have been grateful for the improvement in circulation and the reduction of perspiration in their cold, clammy extremities, but the course of the arthritis has not been modified. Indeed, in several patients the disease has advanced more rapidly in the sympathectomized extremities than in the untreated control ones. These cases have made us realize that, although normal circulation is restored, the arrest or repair of chronic articular disease cannot be counted on. It is therefore logical to recommend sympathectomy in patients with rheumatoid arthritis only if superimposed vasomotor and sudomotor disturbances are a cause of serious discomfort.

IV. Painful Disorders of the Extremities

Painful disorders of the extremities which are discussed in this chapter include causalgia, traumatic arthritis, and the amputation stump neuralgias. In addition to disabling pain these conditions are characterized by trophic disturbances, which consist of edema, glossy skin, muscular weakness, and atrophy of bone; and by disturbances in circulation and sweating. These complications may follow injuries to the nerves, blood vessels, and ligaments. Attention was first directed to the sequelae of penetrating wounds which involve the peripheral nerves in the classic description of Mitchell, Morehouse, and Keen (1864); the rôle of injury to the blood vessels was pointed out by Lériche and Fontaine (1935); and Albert (1936) has emphasized the closely related changes which are associated with trauma to the joints. Frequently the degree of disability and difficulty of treatment form a striking contrast to the insignificance of the primary injury.

Any discussion of this perplexing subject must be prefaced by an admission of how little is known about it. Leriche and Fontaine (1935) have summarized evidence against the existence of special trophic nerves. These writers believe that both trophic disturbances and pain are the result of abnormal vasomotor reflexes. As a result of experiments upon the sensitiveness of parts about an injury Lewis (1937) finds that the pain and vascular flare are related to a hitherto unrecognized set of "nocifensor nerves." He believes that these special fibers belong to the somatic posterior root system and that stimulation of their widely arborized axons, through axon reflexes, in some way lowers the threshold of the ordinary sensory apparatus. Although the nocifensor nerves do not belong to the sympathetic system, their irritation results in reflex vasomotor disturbances. All that emerges from these theories as reasonably certain is that abnormal vasomotor activity usually accompanies the pain.

In studying these patients it is confusing to find that the disturbances in circulation may be either in the nature of vasodilatation or vasoconstriction. Most frequently there is hyperemia in the acute stage, followed by cyanosis, coolness, and excessive sweating of the extremity in the chronic stage. Often the uninjured extremities are involved as well, and we have gained the distinct impression that nervous, highly strung persons with cold, sweaty hands and feet are unusually prone to develop these syndromes after injuries that would have no such effect on a more stable individual. Of course, any form of severe pain will cause reflex sweating and vasoconstriction, and patients who have suffered unremitting pain over long periods of time, often accompanied by one or more ill-advised surgical interventions, are likely to become nervous and psychoneurotic. When the situation becomes further complicated by a "compensation neurosis" or addiction to morphine, even a well trained psychiatrist is often unable to decide whether the pain is functional or organic.

In most instances we have found that the pain has an organic basis. Mitchell, Morehouse, and Keen (1864) have given numerous examples of painful lesions in traumatized nerve trunks. The work of Leriche and Fontaine (1932) and of Albert (1936) has shown the importance of irritated nerve plexuses in the walls of blood vessels and in the inflamed periarticular ligaments as

a source of afferent reflex stimuli. But in every instance these impulses run centrally over the somatic nerves. In the case of the blood vessels this has been proved by Moore and Singleton (1933).* Under such circumstances, what rôle, if any, can be played by the sympathetic nerves in the production of pain? Davis and Pollock (1932) have presented experimental evidence to show that a sympathetic discharge can produce physiological changes in the periphery that are painful and are referred centrally by the ordinary sensory nerves. Whether this explanation be true or not, there is no question that these types of pain can often be relieved by breaking the reflex arc, either by excision of a pathological section of artery (Leriche, Fontaine, and Dupertuis, 1937), by infiltrating the sensitive ligaments of a joint with procaine (Leriche and Fontaine, 1932 and 1937; Albert, 1936), or by chemical or surgical interruption of the sympathetic pathways (Homans, 1940, and Livingston, 1938*A* and *B*).

In the first edition of this book the diagnostic value of blocking the sympathetic supply of the involved extremity with procaine was emphasized. The fact that repeated or even single injections of procaine might give effective lasting relief was then just becoming known. Excellent articles on this subject by Livingston (1938*A* and *B*) and Homans (1940) have recently appeared which give some striking examples of its value. We agree with them that the diagnostic value of procaine block is tremendous. It is usually best to repeat the injection on one or more occasions and also to be sure that sterile saline is not equally effective, especially when there is a question of a functional disturbance. By repeated injections of procaine permanent relief may often be obtained. The criteria for treatment by blocking the sympathetic outflow with procaine, which have been formulated by Dr. Homans and fully corroborated by us, are the following: (1) Completeness of relief over the first period of effective sympathetic block; (2) the persistence of relief for a period of over two hours (prolonged duration indicates that repeated injections will cause further improvement); and (3) more

* Moore and Singleton found in animals that intra-arterial injections of sodium iodide or lactic acid were invariably painful. In the case of a viscus such as the liver, injection of the hepatic artery is no longer painful after resection of the splanchnic nerves and upper lumbar ganglia. In the extremity, however, injection of the femoral artery is still painful after lumbar ganglionectomy, but causes no sign of discomfort after the peripheral nerves have been cut.

prolonged periods of relief resulting from the second and ensuing injections.

When sympathetic block with procaine has given complete relief for only a short period of time, upper thoracic sympathectomy or resection of the second and third lumbar ganglia is reasonably sure to succeed. Another possibility that is frequently mentioned is periarterial sympathectomy. A series of papers beginning with Leriche's (1913) first report and including the convincing articles of Fontaine and Herrmann (1933), Lehman (1934), and Homans (1940) have cited cases of successful treatment with periarterial sympathectomy in these conditions. One of us saw and assisted Professor Leriche in a number of these operations during the winter of 1927–28 in Strasbourg. Just why the periarterial operation should at times be effective no one has been able to explain. Perhaps the most satisfactory explanation is that it has no specific effect either on circulation or pain, but that its action is due to the generalized cutaneous hyperemia which follows the destruction of tissue in any surgical incision (see p. 227 and the illustrative cases below). In this way its effect resembles that of procaine block or foreign protein shock, although it is of considerably greater duration. Because we have believed that any unsuccessful intervention (with the exception of procaine injection) is definitely harmful to the morale of these patients, and because of an increasing confidence that operation on the sympathetic ganglionated chain is a safe and more certain procedure, we have preferred this to periarterial denervation.

In the case in which diagnostic procaine block has been followed by no response or when sympathectomy has failed, what to do next becomes a major problem. When the patient is amenable to psychiatric help in facing his pain or when conservative measures offer any hope, recourse to the major operations on the spine should be avoided. If the patient can be protected against ill-advised surgical procedures, a gradual improvement will often take place. In others, however, surgical relief is a necessity to prevent drug-addiction, degeneration of the personality, or self-destruction. Under these circumstances we cannot overemphasize the futility of posterior root section. After sectioning the posterior roots of the brachial plexus on numerous occasions with a wide margin (from C_3 to T_2) we

have yet to see relief of major amputation stump neuralgia in the upper extremity. Intrathecal injection of alcohol, as proposed by Dogliotti (1931), is occasionally successful and can be tried in cases of causalgia or amputation stump neuralgia in the lower extremity. But section of the spinothalamic tract, as high as the second cervical segment in the case of the arm, is the only measure that can be counted on to give relief. When accurately performed, high spinal cordotomy is capable of removing the sensation of pain up to the fourth or fifth cervical segment, but when the neuralgia extends upward into the shoulder and neck this is not high enough. Recently Schwartz and O'Leary (1941) have suggested the feasibility of cutting the spinothalamic tract in the medulla oblongata and thereby obtaining analgesia as high as the first cervical segment. This operation has just been performed by one of us * and has given most satisfactory relief of an intractable postoperative neuralgia which involved the upper chest, arm, shoulder, neck, and posterior scalp. While it is not justifiable to draw extensive deductions from a single case, we believe that wider experience will show that this is a practical procedure and reasonably free from major complications. If this is borne out, the treatment of intractable pain in the upper extremity which extends up into the shoulder and neck will be greatly simplified.

The basic physiology, pathology, and therapy of the pain and trophic disturbances which occur in causalgia, traumatic arthritis, and amputation stump neuralgia have been discussed together, because these conditions have many points in common. There follows a short description of the three separate entities, accompanied by a number of brief case histories to illustrate the difficulties, as well as the successes, that are encountered in this type of surgery.

Causalgia. Mitchell, Morehouse, and Keen (1864) first described causalgia in soldiers following penetrating wounds incurred in the War between the States, and gave one of the best descriptions ever written. They defined causalgia as hyperesthesia of the hand or foot following an injury in the region of a peripheral nerve. In intensity the pain varies from a trivial burning sensation to a state of torture. The pain is constant and

* This case has not yet been reported, but will be submitted for publication by one of us (White) in the near future.

the patient often suffers severe exacerbation on the slightest physical or emotional stimulus. The sufferer is in a perpetual state of defense and may even protect the extremity from exposure to the air. The skin of the affected area undergoes characteristic changes, becoming red to cyanotic in hue. In some cases the extremity becomes scaly and dry, but more often it is cold and sweaty. With these changes there is a gradual atrophy resulting in a brawny infiltration of the subcutaneous tissue, trophic changes in the nails, and a thin, glossy, hairless epidermis. According to Pollock (1930), Charcot and Vulpian were among the first to describe these pathological changes which may accompany peripheral injuries or chronic sepsis. Babinski and Froment, from their experience with wounds in the first World War, concluded that the coincident vasomotor changes arose from a reflex disturbance of the sympathetic centers. Causalgia most frequently involves the median and sciatic nerves. When the ulnar nerve is involved it is usually associated with an injury of the median or the brachial plexus. Little is known concerning the fundamental cause of this condition, although, as pointed out above, the common vasomotor manifestations suggest an underlying abnormality on the part of the sympathetic nervous system.

As a supplement to the outline of treatment that has been given, the following case histories bring out many points of value. Since our personal experience has not been sufficiently wide to furnish illustrative examples of all the different types of treatment, we have been forced to utilize cases reported by our surgical friends. We take this opportunity to thank the authors for their kind permission to use this valuable material.

Case 1. Treatment by resection of occluded radial artery, reported by Dr. John Homans (1940): "A middle-aged man had suffered an arterial embolism The embolus had become fixed in the left radial artery, which felt like a pencil, and could be followed without pulsation into the anatomical snuffbox. The hand was cool, a little pale, cyanotic and agonizingly sensitive to the touch. Two of the fingers, held partly flexed, were especially blue, cold and so very tender that the man guarded them at all times and refused to allow them to be straightened. When the plugged radial artery was resected under procaine, a sudden and dramatic change occurred. The hand not only felt comfortable to the patient, but could now be freely handled. The color of the fingers at once improved."

Case 2. Treatment by paravertebral infiltration of procaine reported by Dr. John Homans (1940): "A woman of 37 was bitten on the back of the right hand by a dog. A local cellulitis rapidly developed. She entered the hospital twenty-four hours later. Her axillary lymph nodes were enlarged and her fingers stiff. She left the hospital in three days and soon seemed to have fully recovered; but four months later she returned. A few days earlier, the back of the right hand and thenar space had swollen. The fingers were a little bluish. They were *held straight, the thumb adducted* as in a median paralysis, the typical causalgia position. There was a brownish discoloration about the wound, which discharged a little serum. The x-ray showed some decalcifications of the bones and narrowing of the joint spaces. There was an intense hyperesthesia of both hand, fingers and forearm, yet light touch was poorly felt in the area of excessive sensitiveness to scratching or gentle pinprick. The patient was treated by hot soaks, the hand and forearm kept in a sling.

"Two months later, that is, five months after the original injury, the patient was still unable, because of hyperesthesia, to use her hand. . . . The skin of the hand and fingers was smooth. . . . At this time, a sympathetic block of the stellate ganglion completely removed, for the moment, all the sensitiveness to touch, pinching and pinprick. . . . The hand felt dry and hot. From this time on, improvement was steady and in a week or two the woman was at work again."

Case 3. Treatment by cervicothoracic ganglionectomy, reported by Dr. R. G. Spurling (1930): A bootlegger had been shot through the axilla, with injury to the axillary artery. Following this injury his hand became cold, cyanotic, and extremely painful. No relief was obtained by resection of the distal end of the severed artery, ligation of the vein, or by lysis of adhesions about the nerve (except for three days, the period of generalized hyperemia of the extremities which follows any operation). Similar relief of short duration accompanied the hyperemia of foreign protein shock. Following these leads Spurling performed a cervicothoracic ganglionectomy and obtained permanent relief (to date over ten years).

An almost identical case has been reported by Kwan (1935) in which causalgic pain in the upper extremity followed a gunshot wound of the axilla. In this patient, a Chinese soldier, lasting relief followed cervicothoracic ganglionectomy, after neurolysis of the brachial plexus, periarterial sympathectomy, and resection of the axillary artery had failed.

In patients with pain in the foot when *diagnostic* procaine block has shown that sympathectomy will be ineffectual, Sicard's (1916) method of intraneural injection of alcohol or Smithwick and White's (1935) modification of crushing the peripheral

nerves above the ankle may be employed before having recourse to cordotomy. The foot can be rendered insensitive in this way without producing any important motor paralysis, but this is obviously not the case in the hand. Lewis and Gatewood (1920) have reported 3 successful results. However, it should be pointed out that this method frequently fails, both in causalgia and in amputation stump neuralgia. This has unfortunately been our experience. Why interruption of all the known sensory nerves should fail and be followed by continued pain in an insensitive area is not known. The best explanation is that there may be an ascending neuritis, as suggested by Mitchell, Morehouse, and Keen (1864).

In conclusion, it must be admitted that some of the major neuralgias will respond to no peripheral operation. From our limited experience we have come to count on successful relief of major causalgic pain in the lower extremity after a satisfactory cordotomy. In the upper extremity a single incomplete section of the spinothalamic tract at the second cervical vertebra, examined after operation by another surgeon, was a failure. To obtain analgesia of the arm and shoulder by this method is a difficult surgical task. The possibility of cutting the pain tract in the medulla oblongata, mentioned on page 233, opens up a new opportunity for the surgical relief of pain which has spread into the upper cervical segments.

Traumatic Arthritis (Post-Traumatic Painful Osteoporosis). Südeck (1900) first described reflex atrophy of bone as a clinical entity and pointed out that it might develop after fractures, trauma of the articulations, and simple torsion. A year later Kienböck (1901) added further cases and an accurate description of the changes seen by x-ray. Leriche and Fontaine (1930 and 1935), who have made a special study of this condition, have demonstrated its constant association with vasomotor disorders and the effectiveness of sympathectomy in its treatment (see also Leriche and Policard, 1930). Fontaine and Herrmann (1933) of Leriche's clinic and Gurd (1936) have given excellent clinical descriptions of the disease. True osteoporosis is characterized by (1) loss of motor function of the extremity, (2) characteristic decalcification in the roentgenograms, (3) the constant coexistence of vasomotor disturbances, and (4) great

pain. Very frequently no bone is broken, but the patient receives a blow or twist or penetrating wound in the region of a joint, most commonly the wrist or ankle. The immediate disability may be slight, but in the course of a few days the joint becomes swollen, discolored, and intensely painful on any movement. During this early, acute phase there are signs of local vasodilatation (hyperemia and an increase of oscillations). In the later stages the hyperemia may disappear, or actual vasospasm may replace it. At this period the extremity becomes cyanotic on dependency, often edematous, and at times shows the glossy skin appearance which is seen in causalgia. In the early period, the x-ray shows a mottled appearance of the bones due to local absorption of calcium. In the chronic stage there is a general loss of calcium salts, and the normal trabeculation of the bones is lost. The osteoporosis is probably brought on by reflex changes in the vascularity of the bone, as it often appears too rapidly to be due solely to functional disuse.

This syndrome causes a complete disability which is very resistant to ordinary orthopedic measures; it may incapacitate the victim for months and end in bony ankylosis. Experience at Leriche's clinic has shown that post-traumatic osteoporosis responds best to sympathectomy, that the pain is usually relieved immediately, and the undesirable sequelae of the disease are prevented. Fontaine and Herrmann (1933) have presented 22 cases handled in this way. They concluded that cervicothoracic and lumbar ganglionectomy need be used only in the most extensive forms of the disease; that periarterial sympathectomy is usually sufficient for cases with osteoporosis in the hands and feet. Herrmann (personal communication) has had a further large experience with the disease at the Cincinnati General Hospital and is convinced more than ever of the satisfactory results of arterial decortication in this particular condition. A simpler and, we believe, more logical procedure is the paravertebral infiltration of the ganglia which transmit vasoconstrictor impulses to the brachial or lumbosacral plexuses. We believe this should be done as soon as the condition is recognized and that, in the way of prevention, much may be accomplished by employing Leriche's method of infiltrating the sensitive periarticular structures with procaine. Just why such a brief in-

terruption of sympathetic reflexes should be effective is difficult to understand, but its beneficial action is illustrated in case histories given below and also in the sections on causalgia and amputation stump neuralgia.

A. Treatment by Paravertebral Procaine Block

Case 1. Louis G., 44, M.G.H. #304623. This patient had fractured the scaphoid bone in his left wrist five years previously. Following this accident he complained of chronic swelling and a burning, aching pain in the wrist and hand. The bones in his wrist became decalcified Two years before admission the ununited bone fragments were resected.

On admission the left hand was cooler than the right, the hand and wrist were atrophied, markedly limited in mobility, and painful to touch or movement On 2/14/30 a diagnostic procaine block of the left upper thoracic ganglia was performed. The fingers warmed from 74 [illegible] mained free of pain, returned to work as an expressman. The pain did not recur for five months. He then returned and was reinjected with procaine at his own request. Pain again disappeared for six months. At the end of this period pain and limitation of motion were again recurring, so the injection was repeated a third time. Since then he has reported no further trouble.

Case 2. A similar patient with intractable pain following fracture of a carpal bone has been relieved with equal success by a single paravertebral injection of procaine administered by Dr. H. H. Faxon.

Case 3. Reported by Dr. John Homans (1940): "E. A. D., a married woman of 50 or so had long haunted the outpatient department, complaining chiefly of arthritis. Recently, she had suffered a Colles's fracture of the left radius with marked posterior displacement. Reduction secured fair position and the hand was immobilized in acute flexion. Whether it was the initial injury or the flexed position which brought on the subsequent difficulties is not clear . . . the fingers rapidly swelled, pain was severe and the palmar aspect of the wrist *became blistered. A neutral position was at once adopted,* but at the end of six weeks little motion had returned to the fingers and wrist. The hand was painful and edematous. Hyperesthesia of the hand and wrist was extraordinarily severe. The forefinger could not even be touched. A procaine block of the sympathetic supply to the arm completely relieved all pain and sensitiveness, restoring much freedom of motion. The relief was . . . only temporary, but from this time on the patient began to improve. She has since had her ups and downs, but all that is left is a somewhat numb, prickly feeling in the tip of the forefinger and thumb."

One of us (White) has seen an almost identical case in Professor Leriche's clinic treated by periarterial sympathectomy with equally striking results.

B. Treatment by Sympathetic Ganglionectomy

Case 4. Barbara F., 16, M.G.H. #161712. An otherwise normal healthy girl had noticed slowly increasing pain on movement of her left foot. Seven months previously this had become much more severe, so that she could only walk with a limp on account of aching pain in the instep which radiated as high as her knee. The pain was somewhat relieved by elevation and the foot was distinctly moister and cooler than the right (temperature difference of 2 to 3 degrees). X-ray showed a striking decalcification of the bones of the painful left foot. This patient was seen by the arthritic clinic, but no definite diagnosis could be made. There had been no old or recent trauma.

After paravertebral procaine block of the lumbar sympathetic ganglia the temperature of the toes rose 13 degrees and the patient was able to walk and bear full weight on her left foot. A resection of the first to third lumbar ganglia was performed on 5/2/40 by Dr. Edward Hamlin, Jr., since which time the girl has been able to walk freely and without pain.

One of us (White) has performed this operation on a similar patient with painful osteoporosis of unknown origin in which there was no improvement in the first two months. After three years the patient has slowly recovered and is now able to walk. X-rays show a definite redeposition of calcium, but it is doubtful whether this or the relief of arthritis can be ascribed to the improvement in circulation due to the sympathectomy.

As a result of these experiences it is our opinion that paravertebral procaine block is worth a trial in all cases. When it produces immediate, but temporary, loss of pain and vasomotor imbalance, it should be repeated on one or more occasions. For the surgeon who is not skilled in injection technique, Fontaine and Herrmann's experience indicates that periarterial sympathectomy of the brachial or femoral artery may be of value when the arthritic changes are limited to the hand or foot. Sympathetic ganglionectomy should be reserved for those cases in which conservative methods have failed.

Amputation Stump Neuralgia. In the major neuralgias after amputation of a limb the patient commonly complains of severe burning pain in the entire extremity. In addition to the

diffuse pain in his stump the victim may experience the sensation that his foot is being crushed in a vise or his toe nails pulled out by the roots. A very graphic description of this terrible condition has been written by Leriche (1932). One of his patients had submitted to forty-three operations; others starting with an injury in the hand had undergone successive amputations until the shoulder girdle alone remained and was still painful. Many of these sufferers end by committing suicide. Leriche believes that the cause of this condition is a diffuse neuroma which infiltrates the scar, but it is a question whether this is the whole explanation. After one has observed the futility of peripheral intervention in controlling the pain, one begins to believe that there must be a central factor as well.

Our method of handling these cases is as follows:

A. First the peripheral nerves are blocked with procaine. If a neuroma can be felt, it should be infiltrated directly; otherwise the separate nerve trunks in the lower arm or leg may be individually injected. This gives a clue to the course of the pain and on rare occasions gives relief over a period of weeks (see p. 243, Case 6). When a neuroma can be palpated its resection is worth a trial. The operation gives an opportunity to explore the stump, but rarely results in lasting relief. To prevent reformation of the neuroma, Leriche recommends division and end-to-end suture of the nerve at a higher level. With the same purpose in view we have injected the nerve trunk with 95 per cent alcohol, but neither of these procedures has often been successful. Under these circumstances it is quite futile to attempt a reamputation unless the stump is so poorly constructed that revision is necessary for other reasons.

B. The possibilities of peripheral surgery having been exhausted, the rôle of the sympathetic nerves is the next point to investigate. If a clear-cut favorable response is obtained by infiltration of the regional ganglia with procaine, treatment by repeated injections should be given a thorough trial (Case 2). If the relief is complete, but short-lived, ganglionectomy is certainly the procedure of choice rather than the mutilating types of spinal operations. A favorable response may be expected when the stump is cold, discolored, and moist, especially when the patient feels that he is benefited by local heat. This method is more likely to succeed in peripheral amputations, such as finger,

wrist, or foot, than in cases of painful thigh or shoulder stumps (see Cases 3 and 4).

For cases which are not amenable to the above measures, there remain: *

C. Subarachnoid alcohol injection. This method was proposed by Dogliotti of Turin (1931) and has been used in this hospital on numerous occasions. In cases of painful stumps in the lower extremity that have remained intractable to the more conservative measures described, it may be tried before recourse to cordotomy (see Case 5). It must be fully understood, however, that the maximal safe dose of alcohol often fails to produce an adequate sensory loss, and even as small an injection as 1.0 cc. may be followed by paralysis of the bladder.

D. Cordotomy. Section of the spinothalamic tract is an excellent operation for intractable pain in the lower extremity. When all other methods fail, it can be counted on to afford relief with the maintenance of a useful stump for an artificial leg (see Case 6). For relief of pain in the arm and shoulder, however, division of the tract high enough in the spine to produce analgesia of the entire extremity is a difficult matter. A new operation, cutting the spinothalamic tract in the medulla, has been mentioned (p. 233). Observation of our first successful case holds out a distinct hope for a practical method of producing analgesia over the highest spinal segments.

As has been stated, posterior root section is almost certain to fail and should not be used (see Case 7).

A. Treatment by Paravertebral Procaine Injection

Case 1. Reported by Dr. W. K. Livingston (1938*A*): A middle-aged physician developed gas gangrene in 1926, through accidentally breaking a syringe in his left hand which contained a virulent culture of B. welchii. This necessitated amputation of his arm below the shoulder. On the following day he began to complain of pain in his phantom hand. He felt severe pain in his fingers and thenar eminence which at times extended up the entire arm. This sensation increased with exposure to cold, and could be reduced by a hot towel over the shoulder or by a drink of whisky.

In June, 1932, Dr. Livingston infiltrated the region of the left cervicothoracic ganglia with procaine hydrochloride at a time when the pain was particularly severe. A Horner's sign developed and the patient

* Since these operations involve the spinal cord rather than the sympathetic nerves, their technic is not described in this book.

"reported that the individual fingers of the phantom hand began to feel warm and to relax, and for the first time in years he felt that he could move the fingers." Thereafter the pain did not recur with its previous severity and he had a fair degree of relief for six months.

A year later he returned, stating that for several months he had noticed an "increasing tension" in the phantom hand He had just been on a hunting trip and had observed that the stump was often cold and that this had made his pain worse. The stump was very cold and wet with perspiration. Paravertebral procaine block was repeated and again the phantom hand became warm and relaxed. "In the three years that have elapsed since this second injection there has never been a return of his original pain. The stump has remained warm and less sensitive, there is no jerking of the muscles, and he considers himself 'cured.'"

Case 2. Dr John Homans has recently reported (personal communication) a successful result in a painful thigh amputation stump after five paravertebral injections of the lumbar sympathetic ganglia In this case the stump was not cyanotic but was cool, and caused two types of pain: an encircling band and a sense of severe contractions in the phantom toes. With each paravertebral block the symptoms became less pronounced and the ensuing interval of relief lengthened. A new injection was not undertaken until symptoms had begun to recur. Under this regime the pain-free intervals became progressively longer until after the fifth injection relief has been permanent.

B. Treatment by Sympathetic Ganglionectomy

Case 3 Roger P, 30, M G.H. #302151. This patient had crushed the tip of his right index finger in a box-making machine seven months before. The amputation stump of this finger and his entire arm became painful Dull, aching pain radiated up his arm to the axilla and pectoral region He had often noticed that his hand was cold, moist, and cyanotic. Artificial warmth alone gave relief.

General physical and neurological examinations were negative, except that his hands were both cool and cyanotic (right more than left). The amputation stump was not hypersensitive, and there was no palpable neuroma.

Neither injection of procaine at the base of the finger nor exploration and revision of the stump gave relief, but a diagnostic procaine block of the upper two thoracic ganglia produced vasodilatation and stopped the pain for two hours

2/7/30: Resection of first and second thoracic ganglia, right. This gave complete relief of pain.

4/9/32: As in most of the cases when only two ganglia were removed, [illegible] With [illegible] minor

Case 4. Roland L., 29, B.M. #879. The history and physical findings were almost identical with those in the preceding case. A traumatic amputation of the terminal phalanx of the right index finger occurred on March 21, 1930, in a newspaper press. The dull, aching pain in his arm was definitely associated with vasomotor disturbances in his hands.

7/23/30: Exploration and revision of amputation stump by Dr. John S. Hodgson caused no improvement.

11/19/30: Paravertebral procaine injection showed that ganglionectomy should be done to relieve pain.

11/21/30: Thoracic ganglionectomy (T_1 and T_2 R.) with Dr. Hodgson. Uneventful convalescence and relief of symptoms.

C. Treatment by Intrathecal Alcohol Injection

Case 5. Henry P., 24, M G.H. #317313. This man had a Gritti-Stokes amputation in 1931 for gangrene of his right foot due to thromboangiitis obliterans. In March, 1933, his left foot became similarly involved with infection which necessitated a guillotine amputation of the lower leg. A second guillotine amputation above the knee became necessary three weeks later because of further gangrene and infection. This stump at first looked well, but six weeks later became extraordinarily painful. Thereupon the critically low circulation became further impaired and much exudate accumulated over the unhealthy looking granulations.

6/12/33: Lumbar puncture was performed with the patient on his right side and the painful stump uppermost, and 0.7 cc. 95 per cent alcohol injected into the subarachnoid space (Dr. T. J. Putnam).

This injection was followed by hypesthesia to anesthesia of the thigh, lower buttock, and left side of the scrotum and penis. The patient observed a slight reduction in motor power of the thigh, but no difficulty in urination. His stump now remained comfortable and careful dressings could be performed without complaint. The granulating surface then gradually improved and was finally grafted. Nine months later there was still extensive hypesthesia over the original area.

D. Treatment by Section of Spinothalamic Tract

Case 6. William D., 41, M.G.H. #277838. This patient was also a sufferer from thromboangiitis obliterans, who had had a right lower leg amputation in 1926. During the next two months the patient suffered excruciating pain in the stump and was unable to wear an artificial leg. This stump was constantly cold and somewhat cyanotic. He was readmitted to the hospital and treated by local heat, postural exercises, and intravenous doses of foreign protein (triple typhoid vaccine). As all these methods failed, a Gritti-Stokes amputation was finally performed (1/6/28). Circulation at this level remained satisfactory, but he again complained of pain "deep in the knee."

Because the tender area lay directly over the cut end of the sciatic nerve and its injection with procaine had been temporarily helpful, the nerve was exposed at mid-thigh and its trunk injected with alcohol This gave no lasting improvement in his pain. On account of persistent severe pain deep in the end of his stump and inability to use an artificial leg, each of the nerves that reach this region was then blocked in turn with procaine (2/25/29). On infiltrating the region of the obturator foramen, he developed adductor weakness and sudden relief from his pain and soreness. For the first time the patient was able to tolerate pressure on the end of his stump. The relief continued so that three days later he was able to go home wearing an artificial leg. He was then able to work (selling papers) until a year and a half later, when he fell, breaking his artificial leg and traumatizing the stump. Thereupon his old pain recurred. The obturator nerve was reinjected with procaine, but with only temporary relief, so its anterior and posterior divisions were cut between the adductor muscles (6/25/30). The result was disappointing, and the patient was finally submitted to cordotomy by Dr. J. S. Hodgson, who divided the left spinothalamic tract (3/4/31). This operation resulted in analgesia to the seventh thoracic segment and permanent freedom from the pain in his stump.

E. Failure of Treatment by Extensive Section of Posterior Spinal Roots

Case 7. Julius S., 58, M.G.H. #302623. This man fell off a wagon seven years before admission and suffered a compound fracture of his right arm. Gas bacillus gangrene developed and necessitated a guillotine amputation of his upper arm with secondary disarticulation at the shoulder. Within three months pain developed, with twitching sensations in his phantom limb and contraction of the muscles in the region of the stump. This pain became so severe that he had submitted to ten operations (revision of stump, resection of neuromata and of brachial plexus) without benefit. After admission to this hospital he was tested by paravertebral procaine block and subsequently by alcohol injection. As neither method gave convincing relief, posterior root section was carried out on 6/2/31 from the third cervical through the second thoracic segments The anterior roots of the brachial plexus were also divided to stop the twitching of the shoulder muscles. This was successful in putting a stop to the muscular twitchings, but apparently had no effect on the diffuse pain in his neck and shoulder. The patient was followed until his death three years later, but continued to suffer to the end.

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Because the tender area lay directly over the cut end of the sciatic nerve and its injection with procaine had been temporarily helpful, the nerve was exposed at mid-thigh and its trunk injected with alcohol. This gave no lasting improvement in his pain. On account of persistent severe pain deep in the end of his stump and inability to use an artificial leg, each of the nerves that reach this region was then blocked in turn with procaine (2/25/29). On infiltrating the region of the obturator foramen, he developed adductor weakness and sudden relief from his pain and soreness. For the first time the patient was able to tolerate pressure on the end of his stump. The relief continued so that three days later he was able to go home wearing an artificial leg. He was then able to work (selling papers) until a year and a half later, when he fell, breaking his artificial leg and traumatizing the stump. Thereupon his old pain recurred The obturator nerve was reinjected with procaine, but with only temporary relief, so its anterior and posterior divisions were cut between the adductor muscles (6/25/30). The result was disappointing, and the patient was finally submitted to cordotomy by Dr. J. S. Hodgson, who divided the left spinothalamic tract (3/4/31). This operation resulted in analgesia to the seventh thoracic segment and permanent freedom from the pain in his stump.

E. Failure of Treatment by Extensive Section of Posterior Spinal Roots

Case 7. Julius S., 58, M.G.H. #302623. This man fell off a wagon seven years before admission and suffered a compound fracture of his right arm. Gas bacillus gangrene developed and necessitated a guillotine amputation of his upper arm with secondary disarticulation at the shoulder. Within three months pain developed, with twitching sensations in his phantom limb and contraction of the muscles in the region of the stump. This pain became so severe that he had submitted to ten operations (revision of stump, resection of neuromata and of brachial plexus) without benefit. After admission to this hospital he was tested by paravertebral procaine block and subsequently by alcohol injection. As neither method gave convincing relief, posterior root section was carried out on 6/2/31 from the third cervical through the second thoracic segments The anterior roots of the brachial plexus were also divided to stop the twitching of the shoulder muscles. This was successful in putting a stop to the muscular twitchings, but apparently had no effect on the diffuse pain in his neck and shoulder. The patient was followed until his death three years later, but continued to suffer to the end.

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Chapter X

HEAD, BRAIN, MENINGES, AND SPINAL CORD

Carotid Sinus Syndrome. Weiss and Baker (1933) have drawn attention to an unusual syndrome of recurrent attacks of syncope due to an overactive carotid sinus reflex. The investigations of this vasodepressor mechanism by Professor Heymans and his associates in Ghent have been reviewed in Chapter IV (see p. 77). The carotid sinus plexus (Fig. 15), which originates at the bifurcation of the carotid artery and sends filaments to the glossopharyngeal, vagus, and cervical sympathetic nerves, causes a generalized vasodilator response when the blood pressure rises in the carotid bulb. Whereas in normal subjects mechanical stimulation of the sinus causes a fall in systemic pressure of less than 10 mm., the exaggerated drop in the presence of an abnormally sensitive sinus may cause spontaneous fainting attacks and at times convulsions. In Weiss and Baker's cases digital pressure on the hypersensitive carotid sinus promptly induced symptoms identical in every respect with the spontaneous attacks. This abnormal response is either entirely unilateral or much more marked on one side than on the other.

Three types of carotid sinus reflex have been described: (1) asystole or sudden slowing of the pulse with or without fall in arterial pressure; (2) marked fall in blood pressure without pronounced slowing of the heart; (3) changes in the cerebral circulation, causing fainting and at times convulsions, with or without striking alteration in the heart rate or blood pressure.

While the syndrome of the hyperirritable carotid sinus is not difficult to diagnose in its characteristic, fully developed form, this is far from being the case with its less common manifestations. The hyperactive reflex can induce striking changes in the intracardiac conduction system. In addition to complete heart block, these include temporary asystoles of the ventricle with

continued auricular contraction, nodal rhythm, ventricular extrasystoles, changes in the shape of the T-waves, and complete inversion of the electrical axis of the heart. It is also of interest that the irritability of the carotid sinus is increased by digitalis. The possibility of a latent hyperirritable sinus should be borne in mind by every surgeon who operates in this portion of the neck, especially in arteriosclerotic individuals. In freeing the upper pole of the thyroid and in resecting cervical glands this sensitive area is necessarily traumatized and may thereby produce sudden reflex collapse of the patient. Cardiovascular or respiratory collapse of this sort can usually be combated by procaine infiltration or by deepening the anesthesia to depress reflex irritability. Weese (1939) has called attention to the important fact that fatalities may occur during operation upon abscesses in the neck under light evipal anesthesia. The mechanism of death in these cases is explained by the increase in carotid sinus irritability secondary to the inflammatory process and a reflex paralysis of respiration. Evipal should never be used in these cases, but rather an anesthetic like ether by which *sinus irritability is more profoundly depressed. In order to avoid* alarming and sometimes fatal collapse on the operating table, both the surgeon and the anesthetist must be aware of the complications which may arise from an abnormal carotid sinus, and its reflex excitability must be tested before operation (Rovenstine and Cullen, 1939). This should also be carried out by the neurologist in the routine examination of every patient who suffers from convulsive seizures, and by the cardiologist in older individuals who suffer from attacks of heart block and other cardiac irregularities.

In asystole or reflex slowing of the heart, the efferent arc of this reflex is over the vagus and therefore it can be abolished by atropine. The second type of response, which is characterized by a fall in blood pressure, can sometimes be benefited by ephedrine, but the primary attacks of syncope and convulsions can only be treated by denervation of the sensitive sinus.

In selecting patients for operation, infiltration of the sinus with procaine should be carried out as a diagnostic test. Great care must be used not to inject the solution into any of the large blood vessels. The production of a Horner's sign or recurrent laryngeal nerve paralysis indicates a thorough infiltration of

the tissues around the carotid sheath. Under these circumstances all symptoms due to a carotid sinus reflex should be abolished and operative resection of the sinus nerves can be counted on to give a corresponding degree of lasting benefit.

Operation may be performed under the same local anesthetic, or supplemented with ether. In any event, abolition of the reflex irritability of the sinus with procaine is an added safety factor, because severe reflex disturbances set off by the trauma of dissection are thus eliminated. It should be pointed out that reflex irritability is increased by digitalis and by light concentration of many volatile anesthetics. Numerous reports of carotid sinus denervation for syncope and convulsions are now on record and show very satisfactory results: Weiss, Capps, Ferris, and Munro (1936) have reported 10 cases, with lasting relief of seizures in 8; 4 further cases have been described by Freedburg and Sloan (1937). In a recent article by Romano, Stead, and Taylor (1940) abnormal brain waves, which made their appearance on stimulation of the irritable sinus, disappeared after surgical denervation. Even bilateral denervation of the sinus is not dangerous, according to Capps and de Takats (1938) and Craig and Smith (1939). Postoperatively 2 of the patients reported by Capps and de Takats showed a significant postural hypotension, but no elevation in blood pressure or heart rate has been observed after removing these important reflex mechanisms for cardiovascular control.

The following three cases illustrate some of the interesting features of this condition:

Case 1. Dr. Eugene H., 54, B.M. #13939. Arteriosclerotic heart disease, angina pectoris, and carotid sinus syndrome with cardiac standstill and syncope.

The patient, a high-ranking medical officer in the Russian army under the Czar and Kerensky, had seen much active service and been perfectly healthy until the winter of 1936. At that time he began to suffer [illegible] He was seen in consulta- [illegible] ided that his cardiac pain [illegible] urosurgical procedure and he was treated medically. When he reported back a few months later his attacks of anginal pain were about the same, but some of the attacks were associated with faintness. According to his wife he often seemed to have short spells of fainting. It was found that very gentle massage over each carotid sinus induced periods of asystole, in which he lost

consciousness, but had no convulsions. On recording the periods of asystole with the electrocardiogram it was found that they lasted from three to seven seconds. After a dose of atropine (1/50 grain) these were more difficult to produce, but the heart could still be stopped on strong pressure.

The patient has been treated medically by Dr. Sprague. When last heard from three years later he was having less frequent attacks of pain and syncope, and was able to live a fairly comfortable but quiet existence.

Case 2. Socrates G., 62, B.M. #16290. Arteriosclerosis and carotid sinus syndrome with bradycardia, hypotension, and left-sided convulsions

The patient had been in good general health until three years before admission. He then noticed a gradual onset of transient spells of weakness and faintness These were frequently induced by turning his head to the left or by bending his neck backward; they occurred on the average of two to three times a day. He would have to brace himself to prevent falling, and had actually fallen down on a number of occasions. Associated with the general weakness he noticed awkwardness and heaviness in his left arm and leg, with occasional twitchings in the left side of his body. Frequently the attacks gave him a dreaded sense of imminent death.

The general examination of the patient revealed nothing abnormal beyond a mild degree of arteriosclerosis. Neurological examination showed a slight increase in the supinator longus and Achilles tendon reflexes on the left. There were no sensory or motor changes. The blood and spinal fluid Wassermann tests were negative. Lumbar puncture showed an initial pressure of 200 mm but no other abnormalities. X-rays were taken to rule out cervical rib and changes in the skull

On testing the carotid sinus reflex by digital compression it was found that pressure on the right caused a fall in blood pressure from 140/70 to 60/? mm The pulse rate fell from 100 to 60, but there were no other significant changes in the electrocardiogram. Pressure for fifteen seconds caused deep flushing of the face, followed by the symptoms he had complained of in his left arm; when the pressure was maintained for twenty seconds he lost consciousness and had a mild left-sided convulsion. Pressure over the left carotid sinus produced a similar depression of the pulse rate and blood pressure, but much less marked symptoms. After procainization of the sinus on the right, pressure sufficient to occlude the artery could be maintained for a long time without discomfort or any detectable vascular reflex.

The patient was seen in consultation by Dr. R. B. Capps of Dr. Soma Weiss' Service of the Boston City Hospital. He felt that the case was a typical instance of the carotid sinus syndrome with a predominating cerebrovascular reflex. Operation performed on 11/28/34 showed a distinct enlargement of the carotid bifurcation On handling what appeared to be a group of nerve fibers which lay between the two carotid

branches, the patient's blood pressure dropped 60 mm. Procaine infiltrated into this area caused an immediate rise to his normal pressure and prevented any further fluctuation. The bifurcation of the common carotid artery, as well as the lowest 2 cm. of its external and internal branches, were carefully denuded of all strands of nerve and connective tissue in their adventitial layer (see Fig. 85).

Recovery from this operation was uneventful and the patient left the hospital six days later. At that time he was completely relieved of his previous symptoms of weakness and fainting. When re-examined two years later the patient stated that he was well pleased with the result of operation and had had no more of his old seizures. Pressure over the carotid bifurcation could be carried out with impunity.

Case 3. John C., 69, #241410. Arteriosclerosis and bilateral carotid sinus syndrome with bradycardia, hypotension, and petit mal seizures.

A healthy truck driver started to have "fainting spells" in January, 1940. These came on without warning up to ten times a day and forced him to give up his work. The spells consisted of sudden arrest of purposeful activity without loss of consciousness or convulsive movements. He would suddenly stop whatever he was doing, swallow several times, and appear somewhat cyanotic and distressed. Such attacks lasted fifteen to forty seconds. There was no past history of epileptic seizures, head injury, encephalitis, or any symptoms or signs suggestive of brain tumor.

Both carotid arteries were unusually prominent, dilated in the region of their bifurcation, and contained flecks of calcium in their walls. A typical seizure could be induced from massage of the sinus region on either side, but more easily on the left. His blood pressure was 190/90.

Studies were undertaken in Dr. R. S Schwab's laboratory, making simultaneous records with the electrocardiogram and the electroencephalogram during massage of the irritable sinuses The cardiac tracing showed periods of asystole up to 3 5 seconds, while the brain potential record revealed occasional slow waves (5 per second), followed by a marked drop in voltage. Pressure on the right sinus produced identical, but less striking, abnormalities.

Decortication of [illegible] for a distance of 2 c[illegible] was carried out on [illegible] resection of the nerve structures at the region of the sinus itself. In order to do this the ascending pharyngeal artery was ligated and cut, as it originated from this area along with numerous nerve fibers in a network of fibrous tissue. [illegible] was rendered diffi-[illegible] was nevertheless [illegible]

The patient recovered uneventfully. When tested two weeks after operation pressure on the left sinus no longer induced changes in the electrocardiographic or electroencephalographic tracings. Right-sided pressure still caused characteristic objective and subjective effects.

Four months later similar tests showed that the sinus on the left remained unresponsive. Instead of a great many troublesome seizures, the attacks continued to be milder and more infrequent, averaging three per day. These could be induced by gentle massage over the right carotid sinus. Accordingly on 1/9/41 the sensitive zone at the right carotid bifurcation was denervated by dissecting the adventitia and nerve filaments from the junction of the common, external, and internal carotid arteries. Convalescence was uneventful. We were particularly interested to see if bilateral denervation of both carotid sinuses, with the consequent loss of vasodepressor reflexes, would bring about any rise in blood pressure. No such response could be detected, and it must be concluded that there are other reflex regulatory centers which are capable of maintaining a normal vascular tone in man. The patient was discharged from the hospital six days later without having noticed any recurrence of his attacks

When seen two months afterward he had noticed no spells, but his *wife thought that he had had a few minor seizures in his sleep.* Pressure over the carotid bifurcation failed to elicit any form of sinus reflex from either side or to change the normal wave pattern of the electroencephalogram and electrocardiogram.

Epilepsy. Penfield (1933) has stated that "the one constant, visible phenomenon in the brain during an epileptic seizure is cessation of arterial pulsation. The epileptic brain is subject to local vasomotor reflexes such as have never been described in the normal brain." Although active vasomotor control of the cerebral blood vessels is an established fact, it is most unlikely that any such localized response should be mediated by the cervical sympathetic outflow. This focal constriction of cerebral vessels must probably be due to local lesions (Cobb, 1938). As a rule it cannot be prevented by interruption of the cervical sympathetic trunks, but quite frequently it may be corrected by excision of irritable areas in the cerebral cortex. Measurements of blood flow in the jugular vein made by Gibbs, Lennox, and Gibbs (1934) before, during, and after epileptic convulsions have shown that there is no widespread ischemia of the brain preceding or during an attack.

The first recorded sympathectomy was performed by Alexander (1889) of Liverpool for the relief of epilepsy. This operation was carried out on a fairly large number of epileptics by Jonnesco (1896) and other surgeons without striking success Recent anatomical investigation has shown that Jonnesco's operation left the sympathetic rami along the vertebral artery

intact, so that the cerebral vessels were only partly cut off from their vasoconstrictor nerves (Fig. 14). Consideration of these facts led Mixter and White to attempt total sympathetic denervation of the brain by bilateral cervicothoracic ganglionectomy. This was carried out in a series of 17 patients suffering from frequent and severe epileptic attacks. Every case had been subjected to a careful preoperative study by the neurological service, with encephalograms in most instances to rule out localized injury to the brain cortex. None had responded to ketogenic diet or to phenobarbital. These were reported in the 1935 edition of this book. At the time of its publication results in 3 of 17 cases were encouraging. But it was pointed out that the period of follow-up was short and that in the past other entirely non-specific operations, such as colectomy, had produced a certain number of apparently successful temporary results. This conservative attitude was not ill founded, as the final outcome in these 3 cases has been disappointing. We therefore believe that complete sympathetic denervation of the brain has been given an adequate trial and found to be without benefit in the convulsive state.

Migraine. As Harris (1936) has pointed out, it can scarcely be doubted that typical ophthalmic migraine, which is preceded by sudden disturbances in one of the visual fields and other cortical disturbances, must be associated with vasomotor changes in the cerebral vessels, while the succeeding stage of headache is associated with vasodilatation of the middle meningeal, temporal, and other branches of the external carotid artery. Clark, Hough, and Wolff (1936) have demonstrated that this is the mechanism of experimental headaches induced by intravenous injection of histamine and that the pain is caused by stretching of the perivascular plexus of sensory nerves. Nevertheless there is no evidence to prove that either this vasodilator response or its sensory disturbance are carried over cervical sympathetic trunks. Indeed there is every reason to believe that no sensory fibers are transmitted over the superior portion of the cervical sympathetic trunk. We have observed the effect of unilateral cervicothoracic ganglionectomy and of procaine block of these structures on the headaches produced by histamine, lumbar puncture, and pneumoencephalography and have been able to find no evidence that pain is reduced on the denervated side. Fur-

thermore Solomon (1936) was unable to demonstrate any general sympathetic disturbance during the evolution of a migraine headache by such a delicate test as measurement of the electrical resistance of the skin, nor was there any change when the headache was relieved by ergotamine.

It must be admitted that there is some evidence that migraine and other forms of headache may be relieved by sympathectomy, but the reports are too few to be convincing. Love and Adson (1936) studied the patients who had been submitted to cervical or cervicothoracic sympathectomies for conditions other than headache, but who complained of headaches in addition to their primary disease. They were able to follow 16 patients, of whom 12 were either partly or completely relieved and 4 were unaffected. Dandy (1931) and Craig (1935) have each reported 2 cases of severe hemicrania relieved by cervicothoracic ganglionectomy. But if this operation were consistently effective there should be a larger number of enthusiastic case reports. We have tested a number of patients by diagnostic injection of procaine during their attacks. They have developed satisfactory signs of sympathetic paralysis, but without benefit to their headaches —in one patient the headache became definitely more severe.

A most valuable description of the sensory innervation of the dura mater has recently been written by Penfield and McNaughton (1940) which gives the first satisfactory explanation of the propagation of migrainous headache. These investigators have studied the nerve supply of the dura mater in cleared preparations. Their findings in brief are as follows:

> The dura is in large part insensitive, but it contains sensitive areas which coincide with the meningeal vessels and the large venous sinuses.
>
> Stimulation over the course of the middle meningeal artery causes pain which is localized by the patient near the point stimulated. This is transmitted by filaments from the second and third divisions of the trigeminal nerve.
>
> The ache which results from stimulation of the longitudinal and straight sinuses is referred to the forehead and eye, because the innervation of these structures is received from the ophthalmic or first division of the trigeminal nerve.
>
> Stimulation of the sigmoid sinuses and region of the jugular bulb is referred to the region of the mastoid and transmitted over the vagus

When these observations are coupled with the findings of Clark, Hough, and Wolff (1936) that headache is due to ex-

cessive pulsation and stretching of the walls of the dural and temporal arteries, the only reason for supposing that cervical sympathectomy can be of value is the assumption that it causes a reduction of the vasodilator response. There is little evidence to favor this assumption. A far more logical procedure has been proposed by Penfield (1932) and further recommended by Harris (1936) and by Penfield and McNaughton (1940). This consists of selective section of the upper and medial fibers of the trigeminal posterior root, the reverse of the procedure commonly employed in trigeminal neuralgia. This of course interrupts the sensory fibers to the blood vessels of the dura and scalp, which have been shown by Clark, Hough, and Wolff (1936) to play such an important rôle in migraine headache. In Penfield's operation he must have cut the middle meningeal and probably the temporal artery as well, thereby interrupting the pulsations of these vessels, in addition to denervating the major portion of the nerve supply to the dura and tentorium.

In conclusion, it can be stated that available evidence suggests that the autonomic nervous system is implicated in the abnormal pulsations of the cranial branches of the external carotid artery which are so important in migrainous headache. But there is little evidence that these impulses ascend in the cervical sympathetic trunk and none to show that afferent impulses traverse this route (see p. 259). When confronted with further cases of intractable migraine it is our intention to begin our studies with diagnostic injection of the stellate ganglion with procaine. Ganglionectomy will be performed only if unequivocal relief is obtained. Otherwise a trial of cutting the temporal and middle meningeal arteries is recommended as a preliminary procedure, to be followed by section of the upper and medial two-thirds of the trigeminal root if the minor procedure is unsuccessful. Since the section of the root is performed through the same opening made to expose the middle meningeal artery, there is little to be lost by postponing this to a second stage, if it is necessary.

Atypical Neuralgias of the Head. Trigeminal and glossopharyngeal neuralgias are two very definite syndromes. Patients submitting to rhizotomy after accurate diagnosis are consistently relieved. The sphenopalatine neuralgia described by Sluder (1918) is a less definite entity, but pain is referred to the

nore Solomon (1936) was unable to demonstrate any gen-
;ympathetic disturbance during the evolution of a migraine ache by such a delicate test as measurement of the electrical :ance of the skin, nor was there any change when the head- was relieved by ergotamine.

must be admitted that there is some evidence that migraine)ther forms of headache may be relieved by sympathectomy, :he reports are too few to be convincing. Love and Adson 6) studied the patients who had been submitted to cervical :rvicothoracic sympathectomies for conditions other than ache, *but who complained of headaches in addition to* their ary disease. They were able to follow 16 patients, of whom 'ere either partly or completely relieved and 4 were un- ted. Dandy (1931) and Craig (1935) have each reported 2 : of severe hemicrania relieved by cervicothoracic ganglion- ny. But if this operation were consistently effective there ld be a larger number of enthusiastic case reports. We have d a number of patients by diagnostic injection of procaine ıg their attacks. They have developed satisfactory signs of)athetic paralysis, but without benefit to their headaches one patient the headache became definitely more severe.

most valuable description of the sensory innervation of the mater has recently been written by Penfield and McNaugh- (1940) which gives the first satisfactory explanation of the agation of migrainous headache. These investigators have ied the nerve supply of the dura mater in cleared prepara- ;. Their findings in brief are as follows:

e dura is in large part insensitive, but it contains sensitive areas ı coincide with the meningeal vessels and the large venous sinuses. mulation over the course of the middle meningeal artery causes which is localized by the patient near the point stimulated. This .nsmitted by filaments from the second and third divisions of the ninal nerve.

e ache which results from stimulation of the longitudinal and ;ht sinuses is referred to the forehead and eye, because the innerva-)f these structures is received from the ophthalmic or first division e trigeminal nerve.

mulation of the sigmoid sinuses and region of the jugular bulb is red to the region of the mastoid and transmitted over the vagus

hen these observations are coupled with the findings of k, Hough, and Wolff (1936) that headache is due to ex-

sensory nerve endings. They found in cats that they could relieve this pain only through section of the posterior cervical and fifth cranial nerve roots. From repeated disappointing experiences with diagnostic procaine block of the cervicothoracic ganglia and their resection in a number of cases we have been convinced that this is not the usual route pursued by the afferent impulses in atypical neuralgia. Where these impulses run and how to interrupt them still remains an unsolved problem.

The article of Penfield and McNaughton (1940) cited in the preceding section and a still more recent experimental study of headache by Ray and Wolff (1940) may prove to contain a clue to the solution of some of these difficulties. Herein it is shown that the dura in the posterior fossa of the skull is supplied by filaments from the glossopharyngeal and vagus and also by the upper three cervical nerves, whereas the dura which forms the falx and tentorium, as well as that which lines the cranial vault, is supplied by fibers from the ophthalmic division. After operation for neuralgia the upper central portion of the trigeminal root often remains uncut and may transmit painful impulses from the greater part of the interior of the skull. In this connection the history is given of a patient with atypical facial neuralgia of many years' duration. Partial section of the trigeminal root (the fibers from the second and third division) and a subsequent sympathectomy had each given only transitory periods of relief. In performing an intracranial exploration on this patient Penfield found an area of contracting scar in the falx cerebri. Stimulation of this area reproduced the pain, and its resection resulted in lasting relief. Further investigation along the lines suggested by Penfield and his associates and also of the sensory function of the facial (nervus intermedius) offers a promising outlook for further clarification of these perplexing problems.

Pseudomotor Responses. Three interesting varieties of involuntary movements of the muscles of the face and tongue, which may occur after injury to the oculomotor, facial, or hypoglossal nerves, have been known for many years under the names of the physicians who first described them. These are the: (1) Marcus Gunn (1883) phenomenon, in which the outer corner of the eyebrow is drawn up when the patient chews; (2) Heidenhain (1883) phenomenon, where the upper lip is re-

region behind the nose and eye, and at times spreads over the entire side of the head and neck. It can be diagnosed by the relief which follows infiltration of the ganglion with procaine. These forms of neuralgia constitute distinct entities and can be relieved by standardized surgical procedures.

In contrast to the classical varieties of neuralgia, atypical forms are extremely difficult to diagnose and to treat. The pain may involve the area of the trigeminal nerve, but it is more constant and may even become continuous. It is described as a deeply seated, burning, throbbing, aching pain, which is not limited to the distribution of the fifth cranial nerve, but may involve one entire side of the head and neck. At times even the shoulder and arm become involved. Frequently the great vessels in the neck become extremely tender to palpation. Although the patient does not suffer as excruciating pain at any one moment as the typical case of tic douloureux, yet the constant, unremitting nature of the condition is a cause of real torture. Tinel (1930) has described a patient with this condition which developed following an accident eight months after total resection of the trigeminal root for tic douloureux. Postoperatively the patient had developed a facial palsy, but in spite of the complete paralysis of the fifth and seventh cranial nerves, she continued to suffer. This pain was more severe, but different in character and distribution, radiating over the entire left half of the head and neck.

Largely because no other afferent pathway was known, it was formerly believed that some pain fibers from the face and head might run over the cervical sympathetic trunk. Helson (1932), in studying residual sensation after operation for trigeminal neuralgia in Frazier's clinic, concluded that, besides the deep sensation of the facial nerve (nervus intermedius), certain fractions of temperature sense are transmitted over the sympathetic nerves. He claimed that this route plays an important part in residual pain after section of the Gasserian root and in atypical neuralgia. But attempts to relieve the atypical forms by resecting the superior cervical ganglion have been failures (Frazier, 1928). Davis and Pollock (1932) have presented evidence that this ganglion carries nothing but efferent neurons and that its stimulation causes pain through a metabolic disturbance in the tissues, which in turn results in irritation of the ordinary

sensory nerve endings. They found in cats that they could relieve this pain only through section of the posterior cervical and fifth cranial nerve roots. From repeated disappointing experiences with diagnostic procaine block of the cervicothoracic ganglia and their resection in a number of cases we have been convinced that this is not the usual route pursued by the afferent impulses in atypical neuralgia. Where these impulses run and how to interrupt them still remains an unsolved problem.

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tracted when the second division of the trigeminal nerve is stimulated; (3) Vulpian (1875) phenomenon of paroxysmal vasodilatation of the tongue, in which engorgement and slow movement of the paralyzed side of the tongue take place when the chorda tympani fibers are stimulated.

Lewy, Groff, and Grant (1937 and 1938) have investigated these phenomena in animals and have shown that the pseudomotor reactions which occur in the paretic eyelid, whiskers, or tongue can be reproduced by stimulating the mesencephalic root of the trigeminal nerve. When this group of cells is stimulated, an autonomic efferent discharge spreads over the third, fifth, and seventh cranial nerves and produces a slow tonic contraction of the paralyzed muscles. This is identical with the effect of injecting acetylcholine into the carotid artery under similar conditions (Bender, 1938). These curious syndromes are probably produced in man by movements of the face and jaw muscles with stimulation of the mesencephalic nucleus,* which sets off an autonomic discharge and liberates acetylcholine in the nerve endings of the face and tongue. When this chemical mediator is liberated in the tissues it causes contraction of skeletal muscle fibers which have been rendered chemically hypersensitive by degeneration of their motor nerves.

Grant (1936) has described a patient with congenital ptosis of his right eyelid in whom from early infancy curious associated movements had been observed whenever he chewed. During ordinary conversation they did not take place, but when the patient moved his jaws while eating the eyelid flew up, attracting the amused attention of those about him. Block of the third division and motor root of the right fifth nerve with procaine hydrochloride and subsequently with alcohol stopped the associated movements by preventing voluntary movement of the jaw muscles on the right and interrupting their proprioceptive fibers. Following intracranial section of the third division and the motor root, the "jaw winking" phenomenon was relieved. From the Philadelphia investigations it would appear that the reflex arc consisted of an afferent stimulus propagated

* From a more recent [illegible]
brain were stimulated, C [illegible]
that the region which gi [illegible]
the mesencephalic root o [illegible]
tramedullary portion of the facial nerve.

over the proprioceptive fibers from the pterygoid muscles to the mesencephalic nucleus, and thence an efferent discharge over parasympathetic fibers in the third nerve with a resultant release of acetylcholine. The chemical action of this compound caused contraction of the paralyzed levator palpebrae muscle.

On a somewhat similar principle of breaking an excessive vasodilator reflex in the side of the tongue in the presence of an ipsilateral partial paralysis of the face, Cobb and Mixter (1935) have recorded the successful surgical outcome in a patient with a Vulpian-like phenomenon, in whom the lingual nerve was first injected with procaine and later sectioned in the floor of the mouth.

This woman, who had had an incomplete section of the left trigeminal root performed seven years previously, had developed a postoperative facial paralysis. From this she had partially recovered, but she continued to complain of an atypical neuralgia which involved the left side of her head and neck. As an additional unusual complication she was troubled by her tongue, which developed peculiar spasms on the hypesthetic left side. These were brought on whenever she tried to chew or swallow dry food. Examination showed that the right half remained normal, while the left was turgid; it curled up and squirmed in slow, worm-like movements, which dragged the tongue backward into her left cheek. These attacks lasted several minutes, during which she was unable to speak, and were accompanied by a dull drawing pain in her tongue and throat. Since the lingual spasm was becoming so disagreeable, operation was advised with the knowledge that Vulpian's phenomenon in animals depended on stimulation of the chorda tympani fibers. Accordingly on 11/16/29 Professor Leroy M. S. Miner of the Harvard Dental School resected a segment of the lingual nerve through the floor of the mouth under local anesthesia. Freedom from the pseudomotor attacks has since lasted eleven years.

This human observation differs in only one respect from the pseudomotor phenomena which have been produced experimentally in animals—the striated musculature of the tongue had not been sensitized to acetylcholine by degeneration of the hypoglossal nerve.

On reviewing their cases of atypical trigeminal neuralgia, Cobb and Mixter found two other patients who had been relieved temporarily of their pain by an operation on the Gasserian ganglion, but who later developed a spasmodic contracture of the desensitized half of the tongue. In these others the attacks were merely an occasional source of annoyance which made

speech and swallowing difficult, so that surgical intervention was not attempted.

Two other peculiar autonomic disturbances are seen occasionally after injuries of the nerves in the face: (1) The so-called "auriculotemporal" syndrome follows inflammation or trauma to the parotid gland with injury to the regional nerves. During eating there is pain in the gland with vasodilatation and sweating in the region of the temple. This reaction has been explained by List and Peet (1938) on the basis of hypersensitivity of the cholinergic salivary and sudomotor fibers which react to the chemical mediator substance liberated in the course of mastication. (2) The phenomenon of "crocodile tears" may be accounted for on the basis of injury to the lachrymal fibers in the chorda tympani nerve and the resultant sensitization of the tear gland to the diffuse liberation of acetylcholine which occurs, according to Lewy, Groff, and Grant (1937, 1938), during mastication. This phenomenon has also been ascribed by Ford and Woodhall (1938) and Russin (1939) to aberrant regenerating fibers of the facial nerve, so that some of the autonomic fibers which once entered the chorda tympani in their course to the salivary glands become misdirected and follow the lachrymal fibers over the great superficial petrosal and vidian nerves (see p. 44).

Horner's Sign. This syndrome, which should more correctly be referred to as the sign of Claude Bernard-Horner, denotes a paralysis of the sympathetic fibers to the eyelids and orbit. The condition, which was described in animals by Claude Bernard and in man by Horner,* is commonly supposed to consist of pupillary constriction, ptosis, and enophthalmos. Recent work necessitates some modification of these three cardinal signs and the addition of two others of lesser importance. Mutch (1936), by taking flashlight photographs of patients with cervical sympathetic paralysis, has shown that pupillary constriction gives way to dilatation in total darkness. The narrowing of the palpebral fissure results both from drooping of the upper lid and raising of the lower. Enophthalmos, while definite in lower animals, is apparent rather than real in man. The ques-

* It is of historical interest to record that Hare (1839) gave an accurate clinical description of this sign in a case of tumors compressing the cervical sympathetic trunk a generation before Horner.

tion was settled by placing an exophthalmometer in position during an operation and stimulating the cut peripheral end of the sympathetic trunk. Though dilatation of the pupil occurred at once, no forward movement of the eyeball could be detected. This point has been corroborated by Pochin (1939).

A fourth feature has been described by Byrne (1934) and Cogan (1937) and concerns visual accommodation. Cogan points out that sympathetic stimulation flattens the lens and accommodates the eye to distant objects, whereas the parasympathetic aids in focusing on objects at close range. The effect of sympathetic paralysis is not usually sufficient to make the subject obviously myopic, but is apparent on optometric examination.

A fifth rare component of the Claude Bernard-Horner syndrome has been recently called to our attention by Drs. E. D. Churchill and D. G. Cogan—viz., in congenital cases there may be a striking loss of pigment in the iris.

Horner's sign is seen clinically after any form of cervical sympathectomy, but it is incomplete when only the first thoracic ganglion is resected. Injury to the sympathetic chain below this level causes no oculopupillary change. DeJong (1935), who has written a valuable article on the occurrence of the condition in the clinic, gives the following etiological factors in order of frequency: The most common causes are tumors of the spinal cord, or syringomyelia at the level of the ciliospinal center. Next in order are cervical rib, cervical tumor or enlarged lymph nodes, aortic aneurysm, tumors of the upper mediastinum, disease of the pulmonary apices and, more rarely, radiculitis, disease of the esophagus, and adenoma of the thyroid gland. The condition frequently follows trauma, especially in the form of bullet or stab wounds (Cobb and Scarlett, 1920). A hereditary form of Horner's syndrome associated with unilateral facial atrophy and involvement of the brachial plexus has been described by Wechsler (1927). Lesions causing the syndrome through injury of the descending pathway in the brain stem, medulla, and upper cervical cord have been recorded by Wechsler (1927), Riley (1940), Grinker (1937), Winther (1932), and Foerster (1936).

Exophthalmos. Human exophthalmus is due to retrobulbar pressure. In exophthalmic goiter, however, it was formerly believed that the protrusion of the orbit was due at least in part

to the effect of sympathetic stimulation. For this reason many cervical sympathectomies were performed in the belief that the eyeball would recede (Jonnesco, 1923). This procedure proved unsatisfactory. From the evidence reported in the preceding section it is now realized that the smooth muscle which protrudes the eyeball in animals is rudimentary in man. In addition Naffziger (1938) and Brain (1938) have shown that in thyrotoxicosis the exophthalmos is due to swelling of the retrobulbar muscle cone, and can be relieved only by orbital decompression or by reducing the excessive secretion of pituitary thyrotropic hormone.

Retinitis Pigmentosa. A lasting dilatation of the retinal arteries after cervicothoracic ganglionectomy has been reported by Wagener (1931). Royle (1930*A* and 1932) has utilized this effect in an attempt to improve the blood supply to the retina in cases of pigmentary degeneration. Here the arteries appear as mere threads, and the patient suffers from night-blindness and extreme contraction of his peripheral fields of vision. Royle reports that this operation in 6 cases has produced a moderate improvement in visual acuity, as well as an enlargement of the visual fields. The relief was more marked in younger patients and in early forms of the disease.

In our hands 3 patients submitted for operation by the Massachusetts Eye and Ear Infirmary have shown no demonstrable improvement. These were all young women at a moderately advanced stage of the disease. Further studies on earlier cases have shown no demonstrable dilatation of the retinal vessels after paralysis of the ocular sympathetic fibers with procaine. Verhoeff (1931) has had the opportunity to make a microscopic examination of the eye in this disease. In his description of the pathological changes he states that as the retinal vessels run outward from the optic disc their adventitia increases in thickness. Anterior to the equator of the eye the vessels are converted to solid strands of hyaline connective tissue. With a knowledge of these organic changes in the blood vessels, sympathectomy seems definitely contraindicated for this condition. The lack of favorable reports in current medical journals is evidence that this view is shared by the majority of the profession.

Facial Paralysis Leriche (1926) has advocated superior cervical ganglionectomy in cases of severe facial paralysis to enable

the patient to close his eye. Inability to draw the upper eyelid down over the pupil in order to exclude the light may be a most annoying complication of this condition. Creating a Horner's syndrome by this minor operation paralyzes the tonic innervation of the smooth muscle in the upper lid. The resulting ptosis enables the patient to close his eye nearly completely. Hesse (1930) has reported 8 operations of this type and demonstrated the resulting benefit by a series of photographs. In our hands this procedure has been equally satisfactory.

Value of Sympathectomy in Spastic Paralysis. *a. Animal Experiments.* The complex neurological mechanism which maintains a constant tension in normal resting muscles * has been clarified by the work of Magnus, Sherrington, and others. Release of postural reflex centers causes the excessive tension in spastic muscles after injuries to the motor cortex or the pyramidal tracts. While neurophysiologists today are in agreement that the autonomic nervous system plays no direct rôle in this phenomenon, sympathectomy was formerly advocated by Hunter (1924) and Royle (1924*A* and *B*) for the reduction of excessive muscle tone in spastic paralysis of the extremities. In the first edition of this book the erroneous theories on which this operation was based were discussed at some length. But it was already apparent in 1935 that sympathetic denervation had no direct effect on spasticity and that this form of surgical intervention should be given up.

Royle based his operation of cutting the sympathetic rami to the brachial and lumbosacral plexuses on the following incorrect anatomical and physiological theories: (1) that there are two types of tone—"contractile" and "plastic," the latter particularly being increased in spastic rigidity and tending to fix the limb in a given position; (2) that "plastic" tone is largely a function of the red, more primitive type of muscle fiber † which is innervated by sympathetic fibers; (3) that extensor

* In this chapter the word "tone" is used in the usual loose sense found in the medical literature. The term, although a poor one from the modern physiological viewpoint, has been so generally accepted that it is difficult to avoid its use.

† Skeletal muscles are made up of "red" (fine) and "white" (coarse) fibers. The former type has a slower but more powerful contraction than the latter. In man the two types of cells are always intermingled, but in certain muscles one or the other may predominate. The fine strands are most common in the soleus, the coarse in the gastrocnemius. Recent investigations have not upheld the view that the fine fibers are innervated by the sympathetic.

rigidity in decerebrate animals is greatly reduced by sympathectomy.

The fallacies in these assumptions may be seen from reading the papers of Walshe (1925), Cobb (1925), Davis and Kanavel (1926), Alexander Forbes (1929), and Cobb and Wolff (1932).

1. *The theory that muscle "tone" is made up of two components* was suggested by de Boer (1921) and Langelaan (1922) and further elaborated in the work of Royle and Hunter. But Alexander Forbes (1929) after a long study of the problem has concluded that there is no foundation for the idea that the sympathetic nervous system controls a "plastic" element in muscle tone. This viewpoint has now been generally accepted by nearly all the leading neurophysiologists.

2. The evidence that skeletal muscle fibers are innervated by sympathetic axons depends chiefly on the work of Boeke (1927). Wilkinson (1930), Hinsey (1927), Tower (1931), and Ranson (1933) have not been able to corroborate Boeke's work. Tower in discussing this question stated, "Without exception, every ending seen on a skeletal muscle fiber was formed either by a myelinated nerve fiber or by a non-myelinated branch of such, and degenerative section demonstrated the somatic motor origin of these fibers." Ranson (1933) likewise believes that all the sympathetic axons which are found in striated muscle innervate its blood vessels.

3. Royle's (1924*B*) finding that extensor rigidity in decerebrate goats was reduced by sympathetic denervation has not been corroborated by other workers, viz., Davis and Kanavel (1926), W. B. Carrell (1931) and Bisgard (1931).

If muscle tone were influenced directly by the sympathetic nervous system, its stimulation should produce a clear-cut response. *Neither electrical stimulation nor adrenaline have been* found to cause any change, except in the important experiments of Orbeli (1925) and others who have studied the action of these nerves on fatigue. Here it was pointed out that the sympathetic innervation indirectly affects contraction by reinforcing the irritability and conductivity of skeletal muscle. A number of investigators have corroborated this by demonstrating that, independent of the blood supply, there is a decreased resistance to fatigue in the muscles of a sympathectomized limb (Kuntz and Kerper, 1924); that conversely, the contraction of

an exhausted muscle is increased by sympathetic stimulation * (Corkhill and Tiegs, 1933) or by adrenaline (Gruber, 1924); and that the glycogen content of a sympathectomized muscle is decreased (Herrin and Meek, 1931; Dworkin, Bacq, and Dill, 1931).

In addition to this evidence for the regulation of muscle metabolism by the sympathetic nervous system, these nerves, which cause cutaneous vasoconstriction, carry vasodilator impulses to the working muscles. It is therefore probable that sympathectomy may have a slight secondary effect in reducing hypertonicity both by cutting down the blood supply and diminishing the resistance to fatigue in the spastic muscles. These findings are in accord with the general theory of homeostatic activity of the sympathetic nervous system throughout the body.

b. Clinical Experiences with Sympathectomy in Cases of Spastic Paralysis. Royle (1930*B*) reported his results in sympathetic ramisectomies on 139 patients with varying degrees of spasticity in the muscles of the extremities. Many of these patients were submitted to multiple operations with an extremely low mortality (0.5 per cent). In a general way some improvement was seen in 80 to 100 per cent of cases, while 60 to 75 per cent of the patients operated upon felt that the results were good or excellent.

With the exception of Stewart (1927) and von Lackum (1929), few surgeons have been able to achieve results in any way comparable to those of Royle. Carrell (1931) has given an impartial presentation of his results in 60 cases. He concludes that there may be from 10 to 25 per cent improvement, but that Stoeffel operations (cutting part of the motor branches to the spastic muscles) with foot stabilization give a higher percentage of improvement in a large group of cases. Other reports of extensive series of cases have been uniformly pessimistic. Even the late results in Royle's cases have been reported to be disheartening by three sets of impartial observers. Symonds and a group of distinguished colleagues (1930) examined the cases

* As this phenomenon appears only aft[illegible] lasts the period of stimulation by many [illegible] caused by a chemical mediator produ[illegible] (Wolff and Cattell, 1934). Further evide[illegible] by Cobb and Wolff (1932).

which had been operated on by Royle in England. The only possible criticism of their conclusions is that they are based on *only 6 cases. They stated that:*

"(1) The operation of cervical or lumbar ramisection as performed by Mr. Royle is without effect upon the rigidity from extra-pyramidal disease [e.g. Parkinson's disease].

"(2) The rigidity of pyramidal disease, as seen in conditions of hemiplegia or quadriplegia in children, may be temporarily diminished after the operation. This temporary diminution of tone has been observed in both upper and lower limbs with some improvement of voluntary power. The diminution of tone and improvement of function are, however, short lived, and within a few weeks or months, notwithstanding continuous measures of re-education under experienced medical supervision, the condition of the patient remains as before the operation. In the opinion of several of the surgeons who examined these cases both before and shortly after operation, the diminution of tone was no more than may be seen after any major surgical procedure with postoperative shock.

"(3) The operation therefore appears to have no place of value in the treatment of spastic weakness.

"(4) The observations recorded show that in young human beings the sympathetic fibers play no role of any importance in the maintenance of muscular rigidity, whether this is of the so-called Parkinsonian variety or of the type seen in lesions of the pyramidal tract."

Crothers (1925), in reporting on the results of ramisectomy performed in Boston by Royle two months previously, stated: "In my opinion the clinical results in these [2] cases are at least inconclusive. The physiological changes do not seem to me to be demonstrable."

Hertz (1930), who examined 33 of Royle's cases in Australia, came to a similar conclusion.

Seven cases operated upon at the Massachusetts General Hospital by Dr. W. J. Mixter have similarly shown no improvement to justify such a radical form of therapy. The psychic stimulation derived by the patients from the feeling that something definite was being done for them, coupled with the general medical and orthopedic measures taken during their convalescence gave some at least a subjective sense of improvement. A number were distinctly grateful for the increased circulation in their previously cold extremities. Objectively, however, no definite change was noted in muscular rigidity.

We therefore cannot help but agree with Forbes that sym-

pathectomy for relief of spastic paralysis rests on a wholly inadequate physiological basis, a basis built up of speculation and misinterpretation of experimental evidence. The secondary benefits derived through increasing the cutaneous circulation and the altered muscular metabolism do not justify the severity of the operation.

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Chapter XI

HEART AND AORTA

I. Innervation

Perhaps the first important experiment on cardiac sensation was recorded by Goltz (1863). The experimenter was William Harvey and the subject the young son of Count Montgomery, a friend of King Charles I, who had received a severe wound in the chest as a child. Although the thoracic cavity had been opened widely, the accident had not ended in death, but in healing with the heart exposed in an open hole. On taking off a sort of cuirass, which protected the heart, Harvey saw the exposed beating heart. Touching the heart caused not the slightest sensation. A similar modern observation has been put on record by Alexander, Macleod, and Barker (1929), who studied a patient with open drainage of the pericardium which exposed the lower portions of the ventricles and the diaphragm. They also found the ventricles to be insensitive to touch. Rubbing felt like pressure and heavy pressure and pricking like touch. Heat, cold, and vibrations were not perceived at all, and electrical stimulation evoked sensation only when it produced extrasystoles. *Stretching, pricking, or scratching the parietal pericardium*, however, caused severe pain.

These observations are in line with Lennander's (1901) findings that the viscera are insensitive to cutting, crushing, and even burning, but that the parietal peritoneum has acute sensation. It is now recognized that the physiological stimulus of cardiac pain is anoxemia and the products of fatigue (Sutton and Lueth, 1930; Moore and Greenberg, 1937; Blumgart, Schlesinger, and Davis, 1940).

It has been pointed out in Chapter VI that although the true autonomic fibers carry only motor impulses, all the nerves to the internal organs are mixed nerves and contain a certain

number of somatic sensory in addition to a far greater proportion of autonomic motor axons. Leriche (1925), while operating under local anesthesia, was able to show that electrical stimulation of the upper pole of the stellate ganglion caused radiation of intense pain to the arm, whereas when the lower half of the ganglion was stimulated the patient felt pain over the precordium in the second and third intercostal spaces.

In the classical anatomical texts, from Neubauer's (1772) beautiful plates (Fig. 3) down to the late 1920's, only the cervical cardiac nerves are shown. Three distinct trunks, the superior, middle, and inferior cardiac nerves, are given off from the corresponding sympathetic ganglia and descend to form the deep cardiac plexus. A variable number of small branches join the plexus from the vagi. In certain animals the vagus gives off a distinct depressor branch, but in man this structure is rarely found as a separate entity. Langley (1892), in an investigation of the segmental origin of the thoracolumbar sympathetic nerves, showed that accelerator impulses leave the cord by the upper five pairs of anterior roots and their white rami. He assumed that all efferent impulses then traveled upward in the sympathetic chain to form synapses in the three cervical ganglia and send their postganglionic axons to the heart through the cervical cardiac nerves.

Cannon, Lewis, and Britton (1926), in attempting to prepare a totally denervated heart, noticed that accelerator stimuli of nervous origin reached the heart even after resection of both cervical sympathetic chains down through the stellate ganglia.. Later, White, Garrey, and Atkins (1933) obtained as much as a 58 per cent acceleration in the heart rate on faradic stimulation of the second and third thoracic ganglia after division of the trunk above this level.* The explanation of these findings lies in the existence of the thoracic cardiac nerves which form direct connections between the upper four or five thoracic ganglia and the heart. This important anatomical discovery, which accounts for the failure of many operations in angina pectoris, was made almost coincidentally by Braeucker (1927) and by Jonnesco and Enarchesco (1927), and was later corroborated by Kuntz and Morehouse (1930) (Fig. 16).

* In these experiments all other sources of cardiac stimulation were eliminated by section or atropinization of the vagi, resection of the adrenal glands, and transection of the spinal cord at the third cervical segment

The vasomotor nerves of the coronary arteries, in order to maintain homeostasis, probably function in an opposite manner from that of the cutaneous and splanchnic vessels. Working with dogs, Anrep and Segall (1926) demonstrated by measuring the outflow of the coronary sinus that stimulation applied to the vagi causes constriction of the coronary arteries, and applied to the sympathetic causes dilatation. These findings were confirmed by Gollwitzer-Meier and Krüger (1935), who measured blood flow in the coronary arteries by the thermostromühr of Rein. Greene and Atkins (1931) have found that in dogs adrenaline dilates the coronary arteries. On the other hand, Kountz, Pearson, and Koenig (1934) have made a series of extremely interesting perfusion experiments on the revived human heart and have been able to duplicate Anrep and Segall's findings in dogs only when there was dissociation of auricular and ventricular contraction, so that the rate was not influenced by the nerves. In the normally beating human heart vagus stimulation slowed the rate and increased coronary flow, while sympathetic stimulation accelerated the heart rate and reduced the flow. Further observations on the innervation of the coronary arteries have been reported by Katz and Jochim (1939). From their measurements of changes in coronary flow in a preparation consisting of the fibrillating heart of a dog, they concluded that: (1) The vagi carry only cholinergic coronary vasodilator fibers. (2) The stellate ganglia send to the heart adrenergic coronary dilator and constrictor fibers, both of which are tonically active; but in their opinion the tonic action of these nerves is predominantly vasoconstrictor.

We must therefore admit that no final conclusion has been reached on this problem. It is our personal opinion that the most valid experiments are those of Anrep and Segall and of Gollwitzer-Meier and Krüger cited above. Their determinations were made on relatively normal hearts, whereas findings on such abnormal preparations as the revived human heart and the fibrillating dog's heart must be regarded with a certain degree of suspicion.

The afferent sensory axons from the heart appear to follow essentially the same paths as the efferent supply. The same general principles apply to the perception of cardiac pain as to other types of visceral sensation. These theories have been summarized in Chapter VI. Referred pain of the type described

by Head and Mackenzie is characteristically felt in the skin of the inner surface of the arm and the precordial region. This is frequently associated with tender spots over the chest wall. Weiss and Davis (1928) have shown that this type of pain can be abolished by procaine injection of the cutaneous areas to which it is referred. But there is also a type of pain which travels directly over sensory axons in the sympathetic. Heinbecker (1932) has shown that all the cardiac nerves (with the exception of the superior) contain myelinated fibers of intermediate size and with electrical properties identical with those of nerves which carry somatic sensory impulses.

White, Garrey, and Atkins (1933) investigated the pathways of cardiac pain in dogs. By the use of a preparation suggested by Sutton and Lueth (1930), it was possible to shut off temporarily the flow of blood in the descending branch of the left coronary artery. After acute coronary occlusion unanesthetized dogs showed obvious signs of discomfort * and characteristic respiratory changes within fifteen to thirty seconds; the latter were recorded graphically on a smoked drum. The effects of various neurosurgical procedures on the pain of coronary ischemia were tested in a series of 21 animals. It was shown that cutting the vagi or the upper six pairs of intercostal nerves had no effect on the pain produced by transitory ischemia of the myocardium. Bilateral stellate ganglionectomy resulted in only a slight reduction of the sensory stimulus. On the other hand, dogs showed no sign of discomfort after resection of the four upper thoracic sympathetic ganglia or the upper five pairs of posterior spinal roots These experiments, together with the recent anatomical discovery of the thoracic cardiac nerves, explain why cervical sympathectomies have failed so often to relieve angina pectoris.

The nerve supply of the aorta and other large arteries of the trunk is derived from the paravertebral ganglia in a segmental manner. In contradistinction to the peripheral vascular innervation, the visceral nerves are closely grouped around the blood vessels.

* For want of a better word to describe the characteristic reaction to coronary occlusion of this duration, the phenomena described above will be referred to hereafter as signs of cardiac pain But it is most important to emphasize that none of these animals was ever permitted to suffer acutely, although it was evident in each that this would have occurred if the stimulus had been prolonged.

II. Neurosurgical Treatment of Angina Pectoris

The late Sir James Mackenzie (1925) said that discussions on the painful mechanism involved in angina pectoris were usually futile, as they simply consisted of the replacement of one speculative hypothesis by another. Up to the time of his death in 1925 this criticism was perfectly just. To understand the state of confusion at this period one need only recall the number of operations which had been advocated on the cervical nerves and the divergent theories which had been proposed by their authors. The fact that all these methods were reported to have given good results in some cases and to have failed completely in others added even further difficulties. The reader who wishes to familiarize himself with these different procedures is referred to the writings of Jonnesco (1920), Leriche and Fontaine (1932), Danielopolu (1927), Coffey and Brown (1923), Richardson and P. D. White (1929), and many others. Reid and Andrus (1925) reviewed the various forms of cervical sympathectomy, and Fontaine (1925) and Cutler (1927) made statistical studies of results culled from the general literature. Their independent figures are almost the same and are given in Table IX.

In an attempt to explain the inconsistent results of these op-

TABLE IX. RESULTS OF CERVICAL SYMPATHECTOMY IN ANGINA PECTORIS

	Upper Cervical Sympathectomies			*Complete Cervical Sympathectomy or Stellate Ganglionectomy*		
	Fontaine	Cutler *	M. G. H. †	Fontaine	Cutler *	M. G. H. †
Number of cases	57	53	8	37	27	2
Results.						
Good	66.6%	41.5%	37.5%	56.8%	52.0%	50%
Improved	12 3%	35.8%	——	10.8%	18 5%	——
Failures	5.3%	11.2%	50 0%	8.1%	7.5%	——
Uncertain	5 3%	4 0%	——	5.4%	——	——
Deaths (within 4 days of operation)	10 5%	7.5%	12 5%	18.9%	22.0%	50%

* Cutler's figures for mortality have been corrected to include deaths occurring within the first four days after operation.

† Massachusetts General Hospital. Cases operated upon by Drs. C. A. Porter and E. P. Richardson.

erations, recent anatomical findings should be re-emphasized. It is probable that the Jonnesco procedure of complete cervical sympathectomy and also Leriche's method of stellate ganglionectomy result in an interruption of the major portion of the afferent pathways from the heart in a large percentage of cases. This has been emphasized in an excellent article by Govaerts (1936). But the cervical operation is bound to fail when the accessory pathway through the thoracic cardiac nerves is well developed. Why resection of the superior cervical ganglion alone, as recommended by Coffey and Brown (1923), should relieve a certain number of cases of angina pectoris remains a mystery. No afferent axons have been found in the upper portion of the cervical sympathetic trunk (see Chapter III). The only plausible explanation which has been put forward is that the greater portion of the coronary constrictor fibers run through the superior cardiac nerve, and that its interruption increases the irrigation of the myocardium. In view of recent physiological findings, however, it is questionable whether this explanation can be correct.

In evaluating neurosurgical procedures for the control of angina pectoris in the light of present anatomical and physiological concepts which have been outlined above, three possible points of attack must be considered:

1 Vasomotor nerves: Prevention of vasoconstrictor spasm in the coronary arteries.
2 Motor accelerator nerves. Interruption of cardiopressor reflexes.
3 Sensory nerves: Interruption of pain pathways.

The first of these methods must be regarded as of dubious value, because at the present time physiological evidence concerning the action of the cardiac nerves on the coronary circulation is too conflicting to permit any neurosurgical attempt to increase the blood supply of the heart muscle. Furthermore, even if it were feasible it would not often be a practical procedure, as in the great majority of patients with angina pectoris the resilience of these arteries has been lost.

Concerning the interruption of motor impulses which drive the heart to exceed its limited capacity for work, our experiments show that in order to accomplish this completely it would be necessary to remove all the sympathetic ganglia on both sides

from the inferior cervical down through the fourth or fifth thoracic. A bilateral excision would be necessary because stimulation of the ganglia on either side gives nearly equal cardiopressor responses. It would also be necessary to denervate the adrenal medullas, because Cannon, Lewis, and Britton (1926) have found that the denervated heart is accelerated by minute amounts of adrenine. If this were carried out, the heart would undoubtedly be greatly crippled. Danielopolu in his writings has even advised against removal of the stellate ganglia, recommending only the cutting of their postganglionic rami to the brachial plexus and vertebral artery. This point of view is surely overconservative, as the cervicothoracic and second thoracic ganglia have been excised bilaterally many times in Raynaud's disease with no evidence of impaired cardiac efficiency. This is due to the fact that sufficient cardiac accelerator fibers run directly from the third, fourth, and possibly fifth thoracic ganglia to the heart to enable it to respond to its physiological demands. Our clinical observations have even shown that in the presence of advanced degenerative cardiac disease and angina pectoris all the cardiac nerves can be safely blocked on both sides, leaving the vagi and the chemical action of adrenine and sympathin to regulate the activity of the heart. If one wishes to decrease the motor activity of the heart, the operation of total thyroidectomy recommended by Blumgart, Levine, and Berlin (1933) would still seem to be the best way to do it.

We have always maintained that the logical point for neurosurgical intervention is the sensory pathway, but the problem of what and how much to cut had become hopelessly confused by the inconsistent results of cervical sympathectomy (see Table IX). The only possible conclusion to be drawn from such statistics is that the nerve connections to the heart were only partially interrupted. Mandl (1925) and Swetlow's (1926) method of paravertebral injection of the thoracic sympathetic ganglia and the anatomical demonstration of the thoracic cardiac nerves have pointed out the solution of this difficulty. The experimental observations described above and the excellent clinical results which have followed destruction of the upper thoracic ganglia or the posterior spinal roots have completed the chain of evidence and proved that all cases of cardiac pain can be relieved by properly devised neurosurgical operations. Our present knowl-

edge of the pathways of cardiac pain is illustrated in Figure 54. This diagram shows that sensory impulses traveling in the cervical sympathetic nerves cannot enter the cord until they descend to the level of the highest white rami in the thoracic region.* With this in mind it is clear that the upper thoracic ganglia, their communicant rami, and the posterior spinal roots are the focal points through which all cardiac pain must pass. Destruction of any of these thoracic structures will interrupt the sympathetic afferent pathways from the heart.

During the past thirteen years 74 patients with intractable cardiac pain have been treated along the lines just described at the Massachusetts General Hospital. Patients have been transferred to the neurosurgical service by the cardiac consultants after a thorough trial of medical treatment has failed to bring adequate relief of severe angina pectoris. The only requisite has been really severe and frequent bouts of pain. No patient has been refused surgical treatment because of recent coronary infarction or threatened cardiac failure. Milder cases which could be maintained in even relative comfort on a medical regime have not been accepted. Few were able to perform any kind of work, and 18 were having many attacks while at rest in bed; 26 presented clear evidence of previous coronary occlusion, and a number were in active congestive failure.

In the treatment of these cases surgical excision of the upper thoracic ganglia is capable of giving a most gratifying relief of pain on the side of operation. Prior to 1939 we used the posterior approach described by White, Smithwick, Allen, and Mixter (1933) to resect the central portion of the second rib and the upper three thoracic ganglia, but this operation was found to be dangerous in patients with advanced coronary disease. Although there were no early postoperative fatalities, 2 of 4 patients died within a month of operation; one on the twelfth day of syphilitic occlusion of the coronary orifices, and the other a fortnight after discharge from the hospital of unrecognized

* Heinbecker (1933) has claimed that he has been able to detect direct sensory connections between the cervical sympathetic ganglia and the spinal cord Our experience with cardioaortic pain referred to the cervical plexus has

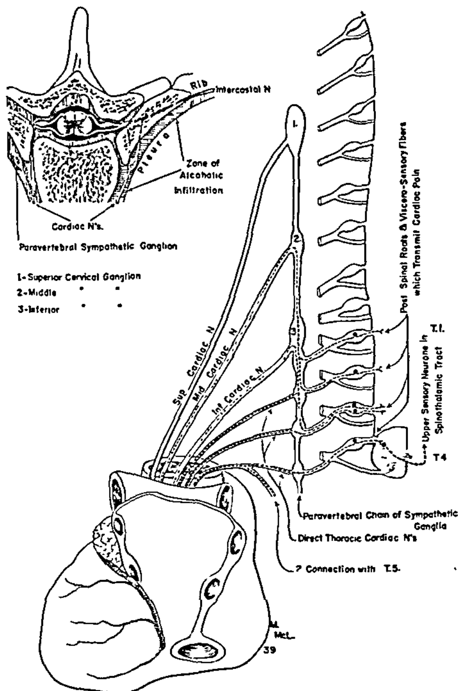


Fig. 54. The sensory nerves of the heart.

In [illegible] fibers from the vagus are not [illegible] un. There are possibly afferent [illegible] they must establish connections with the cranial and upper cervical nerves rather than descend in the cervical sympathetic trunk (see Davis and Pollock, 1932). Although a thoracic cardiac ramus is shown arising from the fourth thoracic ganglion, it is questionable how often it exists. (Reproduced from article by White, 1940, courtesy of *Surgery, Gynecology and Obstetrics.*)

empyema which followed a mild postoperative pneumonia. It is our present feeling that patients with advanced coronary disease should not be operated upon in the prone position. Respiratory exchange is greatly reduced with the weight of the patient on his chest and abdomen; as a result the return of venous blood to the heart is impaired and falls in blood pressure are a common occurrence. This is not the case when operation is performed with the patient on his back. By using the supraclavicular approach, in which the anterior scalene muscle is divided, the apical pleura can be freed down to the third rib and the sympathetic trunk resected from the middle cervical down through the third thoracic ganglion. This approach has given a most satisfactory exposure in the last 2 patients operated upon and is recommended as the procedure of choice in patients who are not impossible surgical risks. A description of the technic of cervicothoracic ganglionectomy by both the anterior and posterior approach is given in Part III. Leriche (see Bérard, 1937), who removes the stellate ganglion alone, has been able to do this in a series of 27 patients without a death. But on account of the fact that accessory fibers in the thoracic cardiac nerves are left intact, Leriche's operation, which is limited to the stellate ganglia, is not consistently successful (excellent results, 26 per cent; great improvement, 15 per cent; improvement, 26 per cent; failure, 26 per cent; result unknown, 7 per cent). Although we have not sufficient cases to prove our point, it is our belief that the additional resection of the second and third thoracic ganglia adds little to the risk of the procedure and will reduce the number of failures to a very low percentage.

Thoracic Ganglionectomy. Protocols of two typical cases submitted to thoracic ganglionectomy are given below. The first illustrates the completeness of the left-sided denervation by the fact that in the eventual fatal coronary thrombosis intense pain involved the right arm and precordium, but never crossed the midline.

Case 1. Giuseppe G., 20, M.G.H. #270156 Rheumatic heart disease, mitral stenosis and regurgitation; also aortic stenosis and regurgitation with angina pectoris

This young man first entered the hospital with rheumatic fever in 1925. At that time he already had signs of cardiac involvement with aortic regurgitation. In 1928 he experienced precordial pain on drink-

ing cold water. Since then the attacks had remained localized to the left precordium, but increased in number and severity. The attacks were particularly troublesome at night (four to six attacks) and lasted as long as an hour.

Examination revealed a pale, thin young man with arterial pulsations in his neck, a thrill over the great vessels, and a systolic and diastolic aortic murmur. There was no evidence of cardiac failure. The heart was moderately enlarged. Electrocardiogram showed a diphasic T_2 and left axis deviation.

1/28/29: Diagnostic procaine block of first and second thoracic ganglia, followed by relief for twenty-four hours.

2/5/29: Resection of central end of second rib with first and second thoracic sympathetic ganglia on left side. Drs. W. J Mixter and J. C. White.

The patient made a smooth convalescence. His left-sided anginal attacks were permanently relieved, but he continued to have mild bouts of pain in his right chest which served as a warning signal. He left the hospital and continued to work as an insurance agent and to lead a fairly active life for the next eight months He was then forced to re-enter the hospital on account of progressive dyspnea. On the third day he developed a fatal coronary occlusion, which was observed from its onset. The remarkable feature of this attack was the distribution of his pain, which was confined entirely to the right side of the precordium and stopped exactly at the midline. Postmortem examination could not be obtained.

The second case illustrates the difficulties which may be encountered by peculiar reference of pain to the head. The typical anginal pain in the chest and arm was relieved by resection of the inferior cervical and upper thoracic ganglia, but the unusual radiation to the upper cervical dermatomes was not interrupted either by resection of the superior cervical ganglion or by subsequent resection of the branches of the superior cervical plexus.

Case 2. Mrs. Elizabeth P., 58, B.M. #187903. Arteriosclerotic and hypertensive heart disease with angina pectoris.

Mrs. P. had an unusual hereditary background of degenerative vascular disease. She herself had had a high grade hypertension for the past twelve years without complications. For the past three years she had suffered from angina pectoris. The attacks, which were entirely localized to the left side, involved the precordium and arm in the usual manner; in addition pain radiated to the forehead, where it was felt behind the eye, to the upper and lower jaws, and also to the neck and posterior scalp. Before entering this hospital she had been treated by rest in bed for several months without relief.

The patient was an intelligent and most coöperative woman of slender build. Physical examination showed tortuous radial arteries

and a blood pressure of 270/130. The heart was just demonstrably enlarged and there were no signs of congestive failure. By x-ray the left ventricle was slightly enlarged and the aortic arch tortuous The electrocardiogram was not quite normal, but showed fair coronary T-waves

5/10/39: Resection of the left inferior cervical, first and second thoracic sympathetic ganglia.

The resection, made through the supraclavicular approach, was followed by an uneventful convalescence. The attacks of precordial and arm pain were relieved, but she continued to feel pain radiating to her neck, scalp, and face.

7/5/39: Resection of the left superior cervical ganglion.

Following this operation, which divided some of the branches of the superficial cervical plexus, the skin of her neck was at first anesthetic. During this period she had no real pain, but noticed clutching sensations in her throat and some discomfort in the left side of her face on over-exertion. As cutaneous sensation in her neck recovered, pain again recurred in this area and became particularly troublesome in the left occipital area. Remembering that she had experienced relief during the period of cutaneous anesthesia, it seemed logical to try the effect of permanent denervation of the area to which this unusual pain was referred

This was accomplished by subsequent resection in two stages of segments of the great occipital and other branches of the superficial cervical plexus, but was followed by only a transitory period of relief. A year and a half later the patient writes that the first operation "removed completely all pain from the lower chest, over the heart, and in the arm . . . I can truthfully say that in spite of the fact that the last two operations have numbed superficial areas, they have not prevented the recurrence of the deep pains" in the base of the neck, chin, and posterior scalp.

In a number of other cases cardioaortic pain referred to the neck has been relieved by blocking the upper thoracic sympathetic fibers (see report of patient with aneurysm of ascending arch of aorta on p. 298). The exact mechanism of the referred cervical pain in the patient cited cannot be explained, but its recurrence in an area of superficial anesthesia is of great importance in the interpretation of theories of visceral pain.

Posterior Rhizotomy. Resection of the upper four thoracic posterior spinal roots should theoretically interrupt the cardiac sensory fibers with certainty and is a standard procedure in which all neurosurgeons are experienced. Since this operation necessitates the prone position and is more time-consuming, we have not yet attempted it. It has, however, been performed 11

times by Davis (1933), Cone, Grant, and Haven * with a single death and with consistent relief of coronary pain.

In reviewing the results of direct surgical intervention it appears that the goal of consistent relief of otherwise intractable angina pectoris is about to be achieved. The older procedures of superior cervical sympathectomy and resection of the stellate ganglion alone fail to interrupt a sufficient number of cardiac fibers and should be given up.† The fear that extensive denervation may result in further damage to the heart with coronary disease (Danielopolu, 1927) appears to be quite unfounded. This is also true of Mackenzie's dictum that surgical relief of pain in angina pectoris, if ever achieved, would be dangerous, because the patient would be deprived of his warning signal. Among the 74 patients treated by surgical and chemical denervation we have now followed a large number in whom all sensation of pain has been removed. Yet these patients always have the sensation of an attack, either from a sense of thoracic oppression without pain, or from palpitation, flushing, or shortness of breath. Direct surgical denervation should therefore be the method of choice for the patient with severe cardiac pain who is a reasonably good surgical risk. Unfortunately the number of patients with the severest forms of angina pectoris who fall into the operable group is limited.

Paravertebral Alcohol Injection. For the treatment of patients with severe coronary pain who cannot safely be submitted to either a thoracic sympathectomy or a posterior rhizotomy, chemical destruction of the cardiac rami by the paravertebral injection of Mandl (1925) and Swetlow (1926) is steadily gaining favor (Bérard, 1937; Ochsner and DeBakey, 1937; Jessen, 1938). The technic employed at the Massachusetts General Hospital has been published by one of us (White, 1940) and is

* With the exception of one of Davis' patients, these cases have not been published.

† It is our belief that this also applies to the operation which has recently been proposed by Raney (1939). This consists of resection of the rami communicantes of the second, third, fourth, and fifth thoracic sympathetic ganglia. The operation necessitates the prone position and requires the removal of the [illegible]

described in Chapter XX. In our experience failure to relieve precordial and arm pain by this method has never been encountered in the presence of signs of an effective paralysis of the upper thoracic sympathetic fibers, i.e., vasodilatation and sudomotor paralysis of the upper extremity and a Horner's sign. While miosis and ptosis are desirable, as they indicate a thorough infiltration of alcohol well up along the lateral border of the first thoracic vertebra, the production of Horner's sign * is

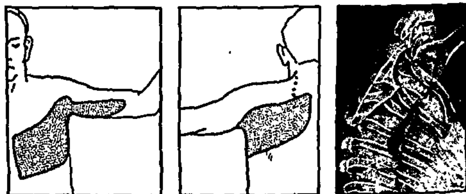


Fig. 55. Points for paravertebral injection in angina pectoris, the resultant area of anesthesia, and distribution of infiltrated lipiodol.

not essential for an effective block of the cardiac afferent fibers. The *sine qua non* is a clear-cut paralysis of the nerves to the blood vessels and sweat glands of the face, neck, and upper extremity.

The points of injection, the resultant intercostal anesthesia, and the distribution of the infiltrated solution are shown in Figure 55. The results in these cases are summarized in Table X. Examination of this table shows that the method is capable of giving really excellent results in over 50 per cent of the cases, and of converting the severe forms of angina pectoris into milder types which can easily be controlled by medical measures in another 30 per cent. In 9.5 per cent pain has not been satisfactorily relieved. In this group the signs of sympathetic nerve paralysis and anesthesia of the intercostal nerves have not been maintained, and it has been evident that failure has been due to the technical difficulty of performing a perfect injection.

* [illegible] t Horner's sign in less than [illegible] tained a hot, dry hand had [illegible] moist and cool within the [illegible]

TABLE X. RESULTS IN 67 * PATIENTS WITH INTRACTABLE ANGINA PECTORIS TREATED BY PARAVERTEBRAL ALCOHOL INJECTION

Complete or nearly complete relief of pain	52.0%
Reduction of severe attacks to a mild form which can be treated satisfactorily by routine medication	30.5%
Unsatisfactory result	9.5%
Died within two weeks of injection	*8.0%*

* One patient left for South Africa within ten days of injection and has been lost track of. The others have been followed over periods ranging from two weeks to eight years.

The reaction to paravertebral alcohol injection is usually so mild that the patients can be out of bed on the following day and rarely require hospitalization for over three or four days. Even with the injection treatment, however, a certain number of fatalities and complications are bound to occur.

The following early complications have been observed in this clinic:

Pleuritic pain has been troublesome in 4 patients within a few hours of the injection. This has appeared as the procaine has been absorbed, and it is surprising that it is not of more frequent occurrence. One, or at most two injections of morphine and chest strapping have invariably given satisfactory relief. Severe pleuritic pain developed during injection in one case. This was probably caused by alcohol leaking into the pleural cavity. It necessitated large doses of morphine, but subsided within six hours.

Pneumonia followed injection in an eighty-five year old woman who was dying of coronary infarction. Injection in her case was undertaken because of the unusual intensity of pain, which had not yielded to large doses of opiates.

Pneumothorax has appeared within a few hours after injection in 2 patients. The cause of this is penetration of the pleura and puncture of the lung, so that air continues to leak from the injured alveoli for a number of hours. In one asthmatic patient aspiration was necessary for the relief of dyspnea.

Although no instance of intrathecal injection has occurred in this series, such an accident has been reported by Molitch and Wilson (1931). We have withdrawn spinal fluid on one occasion, and have always worried over the possibility of infiltrating alcohol into the subarachnoid space. The precautions which can be taken to avoid it are listed in Chapter XX.

described in Chapter XX. In our experience failure to relieve precordial and arm pain by this method has never been encountered in the presence of signs of an effective paralysis of the upper thoracic sympathetic fibers, i.e., vasodilatation and sudomotor paralysis of the upper extremity and a Horner's sign. While miosis and ptosis are desirable, as they indicate a thorough infiltration of alcohol well up along the lateral border of the first thoracic vertebra, the production of Horner's sign * is

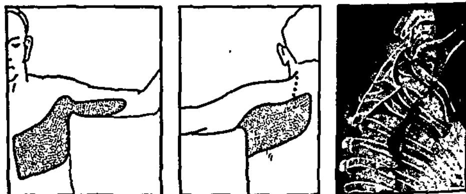


FIG 55 Points for paravertebral injection in angina pectoris, the resultant area of anesthesia, and distribution of infiltrated lipiodol.

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* [illegible] t Horner's sign in less than [illegible] ained a hot, dry hand had [illegible] moist and cool within the [illegible]

disease its disadvantages are far less than the risk of mortality from operation, but it prevents the application of the method to any but the severe forms of angina pectoris.

Five patients have died within two weeks of injection:

1. An 85-year-old woman, moribund from coronary infarction, but with an extraordinary amount of precordial pain, was injected and her cardiac pain relieved. Three days later she died of pneumonia.

2. A 62-year-old lawyer was first seen in consultation with Dr. S. A. Levine at the Peter Bent Brigham Hospital. He had generalized arteriosclerosis and suffered from a rapidly increasing number of attacks of typical angina pectoris (up to twenty in a single night). Electrocardiogram showed abnormal T-waves in the first and fourth leads, consistent with coronary disease affecting chiefly the anterior surface of the left ventricle. After three weeks' hospitalization without benefit from medical therapy, paravertebral injection was performed. Just as the infiltration of alcohol was completed he suffered a syncopal attack with fall in blood pressure to 40 mm. systolic, and a reduction in pulse rate from 120 to 60. His respiration nearly ceased. After oxygen inhalation and stimulating drugs the blood pressure slowly rose to 100/70. On the two succeeding days his temperature rose to 101 degrees and the leucocyte count to 24,600. During the next twelve days he ran a slowly downhill course, with progressive heart failure and electrocardiographic changes typical of extensive coronary thrombosis. Postmortem examination revealed both old and recent infarction of the myocardium.

3. A 65-year old man gave a history of angina pectoris for ten years on an arteriosclerotic basis. Two and a half years prior to admission he had an attack of coronary thrombosis followed by bouts of cardiac pain of increasing frequency and severity. His pain was limited to the right precordium and arm. The electrocardiogram indicated the existence of coronary disease. Paravertebral injection was undertaken after he had failed to respond to medical treatment. The infiltration of alcohol was accomplished without pain or other complication, but ten minutes afterward his speech became confused and his color cyanotic. He rapidly lost consciousness and his heart stopped beating within ten minutes. Permission for an autopsy could not be obtained.

4. A woman of 56 with syphilitic aortitis had suffered from shortness of breath and attacks of substernal pain for three years. In spite of thorough antisyphilitic treatment the anginal attacks had increased in severity and frequency over the past eighteen months. For three weeks she had been in bed with pain in her precordium and both arms, which was precipitated by nervousness, eating, or the least exertion. Nitroglycerine produced an extremely unpleasant sense of fulness in her head. Her blood pressure was 160/50. There were definite enlargement of the heart, broadening of the aortic arch (without aneurysm), and signs of advanced aortic regurgitation without congestive failure.

Another serious early complication is coronary infarction. This has occurred twice in our experience during the course of injection with fatal results, and was probably the cause of an unexplained death which took place on the following day (see section on deaths below). Similar accidents have resulted in 2 other patients a few hours before the time set for injection. John Hunter, an illustrious sufferer from anginal attacks, said that his life was in the hands of anyone who made him lose his temper. His sudden death, which took place after an argument at a medical meeting (Home, 1796), bore out the truth of this remark. If serious coronary insufficiency in the form of either angina pectoris or coronary thrombosis can be precipitated by anger, it is equally likely to be brought on by the emotional strain of a surgical procedure. There is no way to predict this *catastrophe, but much can be done to reduce its likelihood* by thorough preliminary medication, doing the injection with the patient in his bed, and taking care to avoid pain and emotional stimuli.

Late complications have been caused by intercostal irritation and neuritis. The sympathetic ganglia lie so close to the intercostal nerves that alcohol infiltrated around the chain cannot help bathing their trunks. They are paralyzed at first, but anesthesia begins to disappear in their anterior divisions within a fortnight. Within a month the intercostal nerves are recovering along their entire length, and with this there is a greater or lesser degree of hyperesthesia of the chest wall, which commonly persists for a number of months. Most patients state that pressure of clothing irritates the tender skin and that there is a burning sensation with occasional shooting pains. In most cases the discomfort is quite bearable and clears up in a month or two. In others (about 10 per cent) it is more troublesome and requires mild sedation with acetyl salicylic acid or empirin compound, barbiturates at night, and occasional doses of codeine. Baking the hypersensitive areas is often a great help. With the exception of a neurotic woman and one other individual whose injection failed to relieve the anginal attacks, the patients have all stated that they would willingly submit to a second injection if their attacks should ever recur.

There is no question that neuritis constitutes a serious objection to treatment by alcohol injection. In advanced coronary

therefore more easily penetrated by alcohol than are the peripheral nerves, which are thicker and are covered by heavy sheaths of fibrous tissue. An alternative possibility is the fact that even the severest cases of angina pectoris may have spontaneous remissions. In this event a successful block, even if of short duration, may suffice to tide the patient over his period of intractable pain.

Return of troublesome paroxysmal pain after successful injection has been observed in only 6 of the patients in this series. In 2 the recurrent attacks have been so mild that they have been easily controlled by routine medical treatment. In only 4 have they recurred with their previous intensity after intervals from five months to three years. One of these has been submitted to a second injection. This patient, an unusual case where cardiac pain occurred during attacks of paroxysmal auricular fibrillation, has had a second recurrence of rapid irregular beats associated with the anginal pain. Repeated injections of alcohol seem to be less effective, due no doubt to the conversion of the loose retropleural tissue into scar.

The patients with angina pectoris treated by paravertebral injection have become so numerous that it is no longer practical to include the details of the entire series, as was done in the first edition. Instead a number of brief case histories are given to illustrate the various forms of cardiac pain which have been treated and some of the more outstanding results.

Case 1. William M., 54, M.G.H. #280710. Syphilitic aortitis, aortic regurgitation, and angina pectoris.

This patient was the first to be treated by paravertebral alcohol injection. He was a middle-aged carpenter who had had latent syphilis for many years. Nearly three years prior to admission he had his first attack of angina pectoris, and the pains were soon recurring three to [illegible]

was a very loud aortic diastolic murmur, in addition to a moderate aortic systolic and mitral systolic and diastolic murmurs of the Austin Flint type. His pulse was of the Corrigan type and blood pressure 170/35. An electrocardiogram showed inverted T-waves in the first and second leads, with left axis deviation.

The patient was admitted to the hospital, where he was kept in bed on medical treatment for over six weeks. During this period his angina increased in both severity and frequency. The most troublesome

Paravertebral injection was done on the patient's left side in her home in a distant city. The injection was carried out uneventfully, and three hours later she was left in apparently unchanged condition Her local doctor wrote that during the night she awoke sweating profusely and vomiting. There was one attack of pain in her right chest, but none on the injected side. Cyanosis developed, with increasing shortness of breath and a fading radial pulse. She died twenty hours after injection. No autopsy was done, but it seems most probable that her death was caused by a painless coronary occlusion.

5. A fifth fatality occurred in a younger man of 36 with rheumatic heart disease. He suffered from angina pectoris decubitus secondary to destruction of his aortic valve. In addition he had an enlarged heart, orthopnea, signs of mitral as well as aortic valvular disease, and evidence of active rheumatic infection. Paravertebral injection was undertaken because he used up to one hundred nitroglycerine tablets each twenty-four hours and still failed to obtain adequate rest. It was felt that, although he was a distinctly poor risk, his recovery was unlikely unless he could obtain relief from the constantly recurring attacks of pain in his left arm and precordium. Injection of alcohol was uneventful, but he complained afterwards of an unusual amount of chest pain, which required strapping and morphine. The pleuritic pain lasted two days, and although not very severe seemed to exhaust his remaining cardiac reserve and to precipitate decompensation. His discomfort and the signs of decompensation seemed to improve, but he died on the tenth day with sudden cessation of the heart beat. Postmortem examination revealed a moderate amount of free fluid in both pleural and pericardial cavities, but no evidence of thrombosis or myocardial infarct. The usual local reaction to the injection (edema and beginning fibrosis) was noted in the retropleural tissue around the upper thoracic sympathetic ganglia and their rami.

That freedom from severe anginal pain may last indefinitely after paravertebral injection with alcohol is surprising, in view of the fact that after injection of the branches of the trigeminal nerve neuralgia is seldom relieved for more than six months In this series complete interruption of pain has now lasted for over two years in 14 cases, and for more than five years in 3. One patient has been relieved of his former unbearable pain for eight years. The reason for this long lasting paralysis of the cardiac pain fibers is explained by their anatomical structure. The alcohol acts on the delicate rami which unite the sympathetic ganglia with the intercostal nerves dorsally and run ventrally as even more delicate strands to the heart. Whereas the white and gray rami are rarely larger than a millimeter or two in diameter, the cardiac branches are often no thicker than a hair. They are

right. The blood pressure was 150/90. An x-ray of his heart demonstrated no abnormality except a tortuous aorta. The electrocardiogram showed a normal rhythm, rate 75, left axis deviation, and diphasic T_1.

4/25/33: Left paravertebral procaine-alcohol injection, T_2-T_4. The patient complained of very little discomfort from this procedure. He developed a striking vasodilatation of his left hand and cessation of perspiration, as well as a Horner's sign. The postoperative x-ray showed a slight degree of pneumothorax (probably from penetration of the lung during the insertion of the needles), but this subsided within a few days. A letter received six weeks later reported that he had again returned to his practice and was totally free from attacks. Furthermore, he had no discomfort in the anesthetic area in his chest During the next fourteen months he carried on moderately active work and remained free of left-sided angina pectoris. He had, however, noticed the onset of pain in his right precordium. At first this had been a useful warning signal, but lately it had become increasingly severe. He was so pleased with the result of his left-sided injection that he re-entered the hospital on 6/12/34 for a similar procedure on the right. On the day of his admission he had attended his daughter's graduation exercises from college, and noticed an unusual amount of right-sided pain as he walked to his room. At midnight he was awakened by terrific pain in his right chest, which caused him to go into collapse; there was only a slight sense of oppression on his left side. During the course of this attack his blood pressure fell, respirations became labored, and he died three hours later.

Autopsy: There was nothing remarkable outside the heart, which showed diffuse calcification and areas of occlusion and recanalization in both coronary arteries. There was a moderate degree of aortitis and marked scarring of the left ventricle and septum. No recent thrombus could be made out. The only evidence of the old alcohol injection was thickening of the pleura in the region of the second and third thoracic ganglia.

Case 3. J.H.I., 63. Arteriosclerotic heart disease with angina pectoris.

This patient was seen in the University Hospital, Charlottesville, Virginia, in consultation with Drs. A. D. Hart and J. E. Wood. His angina pectoris dated back over an eight-year period, but he was able to get along quite comfortably on medical treatment until the spring of 1935. At that time he had a fairly severe attack of coronary thrombosis, from which he made a slow convalescence. His anginal attacks then became a matter of great difficulty, increasing in frequency up to thirty or forty attacks a day. The attacks radiated to both arms and were especially severe at night. He had been in the hospital for over a month while unsuccessful attempts were made to give him rest at night with oxygen inhalations and opiates.

The patient was obese. He had moderate peripheral arteriosclerosis and a blood pressure of 170/95. The cardiac dulness could not be

feature of his attacks was that they came for the most part at night, so that he became exhausted from lack of sleep. As a result the patient and his physicians finally realized that he would die of exhaustion unless relief could be obtained by surgical means. This led Dr. P. D. White to urge a trial of paravertebral alcohol injection, which had recently been recommended by Swetlow (1926).

2/12/27: Diagnostic paravertebral procaine block T_1-T_5 (left) resulted in freedom from his attacks for thirty-six hours, but not for the long period described by Mandl (1925).

2/21/27: Paravertebral alcohol injection T_1-T_5 (left). The injection was performed without complication and gave the characteristic chest wall anesthesia, but without Horner's sign. He reacted differently from all our other patients in that he noted postoperative attacks of decreasing frequency for two weeks, from which time he had no attack on his left side. He was able to return home and lead a quiet life in comfort.

A year later milder attacks were recurring in his right arm and chest wall. An attempt was made to stop these by a right-sided injection by another surgeon, but this block and another later attempt were unsuccessful. He was then followed in the out-patient clinic and remained altogether free of left-sided pain and without too great discomfort on the right, where the attacks could be relieved by nitroglycerine. Finally in 1933 cardiac failure developed from which he died. No autopsy was performed The relief of his unbearably severe left-sided angina pectoris had lasted over six years.

Case 2. Dr. William N , 58, B.M. #9647. Arteriosclerotic heart disease, coronary occlusion, and angina pectoris.

A physician, who had enjoyed excellent health, began to notice precordial pain on exertion at the age of 43. Two years later he had a coronary infarct, followed by an embolus to his popliteal artery. He was incapacitated for three months, but recovered sufficiently to be able to return to his practice During the past eleven years he had been fairly active, but had suffered from frequent attacks of angina pectoris. The pain was substernal and radiated to the left precordium and arm. He obtained quick relief from nitroglycerine until four months prior to his admission, but at that time he had a series of unusually severe attacks lasting one to two hours and requiring morphine for relief. Three days before entry one of these attacks lasted four hours. As all medical measures had failed, paravertebral injection was recommended by Dr. P. D. White. The patient's father had died of coronary thrombosis and his mother of arteriosclerosis. His own past history was not [illegible]

[illegible] is cardio- [illegible] veins of his neck, nor any evidence of congestive failure. His heart measurements showed that his apex was 9 cm. to the left of his sternum and just outside the midclavicular line. There was no enlargement to the

this latter component of the patient's discomfort which remained uninfluenced by the drug and for which morphia was required frequently.

5/31/34: Paravertebral alcohol injection, T_1-T_4 (left).

There resulted a well-marked Horner's syndrome, a transient partial anesthesia over the left chest anteriorly, and a variable paresthesia over the left upper back and down the inner aspect of the left arm. This was followed by complete relief from the anginal pain during frequent subsequent attacks, the presence of which was made known by a tightening sensation in the throat and a persistence of the accompanying palpitation, respiratory discomfort, and generalized flushing of the skin. However, another important element in addition to the pain had been dispelled; namely, the fear of an impending attack. It is of considerable interest that the precordial ache, which previously had not responded to nitroglycerine, persisted off and on in a modified form, but on the whole was less severe and less frequent. This component appeared to be directly related to the active rheumatic disease and subsequently entirely disappeared. The patient was seen at frequent intervals, and was examined in June, 1936, two years after the injection. She was in good condition and was free from clinical and laboratory evidence of active rheumatic infection. There remained a slight residual Horner's syndrome and a vague sense of numbness to touch over the precordial area, with slight paresthesia along the inner aspect of the left upper arm. She led a quiet life and was able to do light household work. About once a week she had to pause for a few minutes because of tightening in the throat and thumping of her heart, but this was now always related to unusual exertion or excitement.

Nearly four years after the injection the patient developed subacute bacterial endocarditis, from which she died. She remained free of her old anginal attacks throughout.

When allowance is made for the type of patient dealt with, it is evident that paravertebral alcohol injection, in comparison with surgical denervation, carries the minimal risk and with only a slight sacrifice in effective results. However, injection must be performed with the most scrupulous technic in order to place the alcohol with sufficient accuracy to insure destruction of the sympathetic rami and the cardiac nerves. As mentioned below, animal experiments have shown that 5 cc. of alcohol produces an area of necrosis not much over 1 cm. in diameter. Observations made during two postmortem examinations have shown that this applies to man. The infiltration of alcohol must therefore be far more exact than when procaine is used, as this drug diffuses so much more widely through the retropleural tissues. It is always evident when the alcohol has been correctly placed because of the unequivocal signs of paralysis of the upper

determined with great accuracy, but it was thought that the heart was enlarged. Its sounds were of fair quality and there were no murmurs.

As it was felt that the patient could not long survive the exhaustion brought on by his loss of sleep, it was hoped that bilateral alcohol injection might give him much needed relief.

10/8/35: Paravertebral alcohol injection, T_1-T_4 (left).

10/9/35: Paravertebral alcohol injection, T_1-T_4 (right).

The patient came through both injections with a minimum of discomfort and proceeded to recover in a way that exceeded all our hopes He never had another attack of cardiac pain, but continued to have a satisfactory warning signal, which consisted of a sense of oppression in his suprasternal notch. With adequate sleep he was soon able to leave the hospital, and in a remarkably short time to resume mild activities in his store. When seen six months later he remained at work and free of pain. Unfortunately, ten months after injection he had a flare-up of an old subacute cholecystitis, for which his medical advisers were not consulted. Operation, which was performed at another hospital, resulted in an early death from congestive failure

Case 4. Evelyn C , 26, M.G.H. #337315. Rheumatic heart disease with aortic stenosis and angina pectoris. (This patient has already been reported by Bland and White, 1936.)

The patient had rheumatic heart disease with marked cardiac enlargement, free aortic regurgitation with a blood pressure of 170/50, mitral stenosis and regurgitation, and angina pectoris decubitus. Severe rheumatic fever and heart disease began at the age of 9 years. A recrudescence of rheumatic fever occurred at the age of 16, requiring hospitalization for twelve months. She subsequently did well and remained free of symptoms except for moderate exertional dyspnea and palpitation until December, 1933, when at the age of 26 she re-entered the hospital with another recrudescence of rheumatic fever. While at rest in bed she began to have severe angina pectoris. Her attacks were characterized by paroxysmal discomfort due both to pain and to associated circulatory phenomena. The sequence of events began with consciousness of forceful regular heart action and a sense of throbbing in the throat, accompanied by an increase in the pulse rate from a resting level of 90 up to 130 or 140 per minute In one to two minutes an aching precordial pain appeared, rapidly becoming severe and spreading upward in the chest and down the left arm as far as the wrist. Respiratory discomfort and a sense of choking were usually present, as well as profuse sweating and generalized flushing of the skin. A blood pressure determination was not made during an attack. Occasionally dyspnea and palpitation occurred without pain, but never the reverse. Although precipitated by emotion or exertion, the attacks most frequently occurred without provocation, especially during the night. The severe anginal pain was usually superimposed upon a less intense precordial aching sensation similar to that frequently described by patients during active rheumatic fever. Nitroglycerine gave partial relief, but it was

chest, shoulder, neck, and scalp—i e., over the cervical as well as the highest intercostal nerves (Fig. 56). All pain was relieved *for thirty-six hours by paravertebral procaine injection of the* first and second thoracic ganglia, although there was no detectable anesthesia of the skin. A subsequent injection with 95 per cent alcohol gave the patient complete relief for the remaining three months of his life. In this instance right-sided pain was caused by an aneurysm of the ascending arch of the

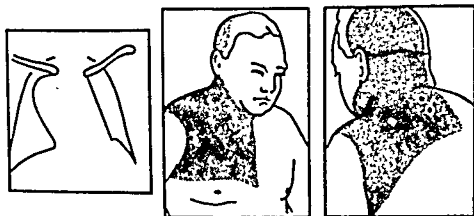


Fig. 56. Aneurysm of ascending arch of aorta.

Stippled area represents region to which pain was referred The black dots mark the points of insertion of needles for paravertebral injection of upper two thoracic ganglia.

aorta, whereas in the two subsequent cases the aneurysms involved the transverse and upper portions of the descending arch. Here the pain was left-sided. These patients were all given satisfactory relief, which in the case of the longest survivor lasted for five and one-half years. Reichert (personal communication) has relieved the pain from an aneurysm in the lowest portion of the descending arch of the aorta by injecting the second to sixth sympathetic ganglia. Eleven months after injection this patient remained free of pain and had returned to active work.

IV. Operation on the Cardiac Accelerator Nerves in the Cardiac Arrhythmias

Over seventy years ago the following quotation appeared in Edes' book on the physiology of the sympathetic nervous system (1869): "Hyperkinesis cordis, or nervous palpitation of the

thoracic sympathetic rami. When these signs persist, pain is just as effectively relieved as though the same structures had been resected.

In summarizing our experiences with the neurosurgical treatment of the most severe forms of cardiac pain, we wish to point out that surgical resection of the inferior cervical and upper three or four thoracic ganglia, or posterior rhizotomy of the corresponding spinal nerves, are unquestionably better methods of dealing with cardiac pain than is paravertebral alcohol injection, provided the patient can tolerate an operation of such magnitude. Surgical denervation causes no neuritis and destruction of cardiac afferent pathways is nearly certain, but many of the severest sufferers from angina pectoris are impossible risks for surgery, and even in the most carefully selected group there will be an occasional fatality.

In choosing between surgical and chemical denervation much depends on the training of the surgeon. Cutting the posterior spinal roots or cervicothoracic ganglionectomy falls within the routine operations performed by the neurosurgeon. But the technic of paravertebral alcohol injection is more difficult to learn and requires frequent repetition in order to perfect it. Satisfactory results can be obtained in no other way, nor can really serious complications be avoided. Mastery of the technic is well worth the effort required, because it enables so many otherwise hopeless patients to acquire relief from their pain.

III. Neurosurgical Relief of Pain in Aortic Aneurysm

Most aortic aneurysms are not acutely painful, but cause symptoms only through pressure on neighboring structures. At times, however, they may produce intense suffering. In our experience this has been particularly true when the aneurysm is situated in the aortic arch and is expanding upward into the outlet of the thorax. It would be logical to suppose that under these circumstances the pain is caused by pressure on the parietal pleura and the intercostal nerves. In order to test the pathway of pain sensation one of us (White, 1932) performed diagnostic procaine block in 3 patients with large and intensely painful aneurysms of the aortic arch. The first case was particularly interesting because the pain was referred to the right upper

Bilateral paravertebral injections were performed with alcohol (2/8/36 and 2/20/36) in the hope of stopping both her cardiac pain and her bouts of fibrillation. This result was achieved, but not permanently. A year and nine months later she returned to the hospital. At this time she was able to stop recurrent attacks with five quinidine tablets, but these gave her so much diarrhea that she requested reinjection. This was again done bilaterally (12/1/37 and 12/4/37) with very little discomfort. Again she experienced relief from both her pain and fibrillation, but this time it lasted for only a month. It has been our experience with reinjection that when alcohol block has once failed, retropleural fibrosis renders ensuing nerve injection increasingly difficult.

In drawing conclusions from published case reports and our own experience, there is good evidence that both paroxysmal auricular tachycardia and fibrillation can frequently be stopped and their further recurrence prevented by chemical or surgical interruption of the cardiac accelerator nerves. It is recommended that a diagnostic injection of procaine be performed first in every case. This will help determine whether normal rhythm can be restored and whether the accelerator fibers must be interrupted on one or both sides. If the abnormal rhythm recurs, injection with alcohol should be tried in individuals who have serious coronary disease, but in all others surgical resection of the inferior cervical and upper thoracic sympathetic ganglia should be carried out by the supraclavicular approach as the method of choice.

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being taken (Fig. 57). Within a few minutes there was an extraordinary change in the heart rate, which fell from 210 beats per minute to a normal rhythm of 83. During the transition there were periods of asystole alternating with short intervals of tachycardia.

6/19/33: Paravertebral alcohol injection, T_1-T_4, under gas-oxygen anesthesia.

The boy remained free of tachycardia for three weeks, then had a very severe attack. He was admitted after two weeks with cardiac decompensation. The signs of complete sympathetic paralysis had disappeared. Reinjection of procaine again stopped the attack.

Two days later the child suddenly died.

Autopsy showed death to be due to a cerebral embolus and hemiplegia. The source of this was a mural thrombus in the left auricle; otherwise the heart was grossly normal.

From the experience gained with this patient, we believe that future cases that respond so well to procaine should have the ganglia resected, provided the patient is a safe operative risk. Alcohol injection in a young child must be done under a general anesthetic. Under these circumstances it is very difficult to produce a permanent sympathetic paralysis, because evidence of accurate placement of the needles cannot be obtained (see p. 444). The difficulties encountered in obtaining a sufficiently complete chemical block to interrupt the cardiac accelerator fibers permanently are further emphasized in the following case, in which advanced coronary disease rendered surgical resection out of the question.

Case 2. Mrs. Abigail W., 69, B.M. #8387. Irritable heart with paroxysmal auricular fibrillation, coronary disease, and angina pectoris.

The patient, referred by Dr P. D. White, was a stout elderly woman, who had noted attacks of rapid, irregular beating of her heart for nearly twenty years. In 1934 these episodes occurred with increasing frequency, and with them she began to suffer from precordial pain with radiation to both arms. Nitroglycerine gave no relief. These attacks lasted from a few hours to several days, but their duration could be reduced by quinidine. This drug, however, caused troublesome intestinal upsets.

On physical examination the patient was found to have generalized arteriosclerosis and a blood pressure of 120/40. The heart was slightly enlarged to the left. During an attack the rate was about 140 and the sounds very irregular in force and rhythm. There were no signs of congestive failure. Electrocardiogram showed flat T_1, sagging T_2 and T_3. In lead 4 the T-wave was diphasic, with the initial phase inverted.

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CHAPTER XII

HYPERTENSION

I. Introduction

MANY attempts to modify the course of hypertension by interruption of sympathetic pathways to large portions of the vascular bed have been made in the past six or seven years. Stimulated by the failure of medical treatment, and by the success which has greeted surgical intervention on the sympathetic nervous system in the treatment of peripheral vascular disease, some progress in this form of therapy has been made. The primary purpose of this chapter is to evaluate the results of surgical treatment to the present time. Before doing so, however, it is desirable to review briefly the experimental and clinical data of the past few years which are responsible for the present concept of the mechanism whereby hypertension is produced in animals and perhaps in man.

There are many causes of and diseases associated with hypertension in man. Page (1939*A*) has classified and listed some fifty of these under five headings: renal, cerebral, cardiovascular, endocrine, and unknown. The first four groups contain many generally recognized disease entities such as chronic nephritis, chronic pyelonephritis, intracranial tumors, coarctation of the aorta and tumors of the pituitary or adrenal glands. All of these conditions must be excluded before a diagnosis of essential or malignant hypertension can be made. The latter are the sole members of the fifth or unknown group in Page's classification and are the ones with which we are primarily concerned in this discussion. Numerically, however, this last group is the largest of all. As a cause of death it has been said to exceed cancer in importance. Allen and Adson (1940), referring to Barker (1937) and Fahr (1928), estimate that hypertension is from two to three

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significant disturbance of renal excretory function, and autopsy revealed no lesions of the arterial tree except in the arterioles of the eye. Other animals in time did develop degenerative arteriolar changes, without significant changes in renal function. These were most marked in the eye, but occurred in other organs and in voluntary muscles, and consisted chiefly of thickening of the musculature of the media. No changes in the renal vessels have been noted.

Constriction of the main renal artery of one kidney results in a temporary elevation of blood pressure, which usually returns to normal in a few weeks.* This may be due in part to the development of a collateral circulation, but more likely to the presence of the other normal kidney. When the latter is removed (Blalock and Levy, 1937; Katz, Mendlowitz and Friedman, 1938; and Goldblatt, 1938A), persistent hypertension usually follows, without disturbances of renal excretory function if the degree of constriction has not been excessive. Release of constriction, or removal of the clamp, or excision of the kidney at the height of the elevation of blood pressure, usually results in a persistent fall to normal levels. That unilateral renal disease in man may be responsible for hypertension is now appreciated (Freeman and Hartley, 1938; and Blatt and Page, 1939), and a number of instances are on record (Butler, 1937; Barker and Walters, 1938; Boyd and Lewis, 1938; Leadbetter and Burkland, 1938; Barney and Suby, 1939; and McIntyre, 1939) where unilateral nephrectomy has resulted in a significant reduction of blood pressure. These cases are not common, and it would appear that a successful outcome occurs when the patient is young, the renal disease and hypertension are both of short duration, and the other kidney is free from disease (Palmer, Chute, Crone, and Castleman, 1940; and Schroeder and Fish, 1940).

If both main renal arteries are excessively constricted, severe hypertension results (Goldblatt, 1940). Renal excretory failure develops, and death occurs in a few days. Pathological changes in the extrarenal arterioles and small arteries are found which are identical with those of the malignant phase of human essen-

* Blalock, Levy, and Cressman, 1939, have shown that unilateral renal ischemia superimposed upon intestinal ischemia results in prolonged elevation of blood pressure in a high percentage of animals. The significance of this observation is not clear. It suggests that extrarenal vascular changes enhance the production of renal hypertension.

times more deadly than cancer. Although its etiology is still a mystery, a good deal is known about the natural history of the disease. If patients are divided into four groups according to the severity of the disease at the time the diagnosis is made, Keith, Wagener, and Barker (1939) have shown that mortality in four years is 30 per cent in the first group, 42 per cent in the second group, 78 per cent in the third group, and 98 per cent in the fourth group. It is probably fair to state that as yet no form of medical treatment has been found that significantly alters the progress of the disease.

II. Rôle of Ischemia in Renal Hypertension

Experimental Constriction of Renal Arteries. A survey of recent literature reveals that experimental hypertension of renal origin resembles essential and malignant hypertension in man. Goldblatt (1940) reasoned that if these forms of hypertension were the result of renal vascular disease, the latter must precede the hypertension and the extrarenal vascular changes which are associated with it. The effect of renal vascular disease, he presumed, would be renal ischemia. He reasoned that by varying the degree of renal ischemia, it should be possible to produce a situation in animals which would resemble both the benign and malignant phases of essential hypertension in man, with and without accompanying renal excretory insufficiency. Goldblatt * and his co-workers (1934–1940) have published the results of their studies in which the renal blood flow was altered by means of a metal clamp placed upon the renal arteries or the aorta. Many different experiments are reported. Their work has been thoroughly corroborated with and without variations by others (Elaut, 1935; Page, 1935*A*; Wood and Cash, 1936; Katz, Mendlowitz, and Friedman, 1938; and Katz, Friedman, Rodbard, and Weinstein, 1939). In brief, it has been shown that persistent hypertension can be produced without impairment of renal excretory function by constricting the main artery of both kidneys, or by constricting the main artery of one kidney and excising the other. Release or removal of one or both clamps results in a slow or rapid return of blood pressure to normal. After five years of hypertension in some animals, there was no

* A preliminary report was made before the Experimental Section of the Academy of Medicine, Cleveland, November 11, 1932.

Pithing was the only operation that produced a moderate fall in blood pressure, but despite the destructiveness of the operation hypertension remained (Glenn, Child, and Page, 1938).

All these observations prove that a nervous reflex from the kidney plays no part in the increased peripheral resistance which results in hypertension. It further shows that in dogs denervated vessels are no less susceptible to the constricting agent (humoral) than those which are normally innervated. It suggests that if human essential hypertension is caused by a similar humoral substance, sympathectomy will not be effective unless it in some way alters the mechanism responsible for the change in renal blood flow, which in turn results in the elaboration of the pressor substance. To quote Goldblatt, "these experiments do not exclude the possibility that in human essential hypertension stimuli from the central nervous system may play an accessory, or, in some cases, even a primary part in elevating blood pressure." These experiments, furthermore, have not proved the necessity for renal vascular disease as a prerequisite to hypertension. In fact, the absence of renal vascular disease in the ischemic kidney comparable to that seen in man with essential and malignant hypertension is repeatedly stressed by Goldblatt. They have shown, on the other hand, that an alteration in blood flow to the kidney will result in persistent hypertension presumably due to the elaboration by the kidney of a pressor substance. The inference that this may also be true in man is clear. The cause of altered renal blood flow in man is not clear, and nothing in these experiments seems to cast the slightest bit of light upon this matter.

Hypertension Due to Cellophane Perinephritis. As has been indicated above, hypertension may not persist when the main renal arteries are compressed if an adequate collateral circulation to the kidney is formed. In order to prevent this, Page (1939*B* and *C*; Graef and Page, 1940) applied cellophane and later silk wrappers about the kidney. They found that this not only prevented the development of collateral circulation, but resulted in a constrictive perinephritis. A fibrous capsule 4 to 5 mm. in thickness surrounded the kidney and was found to be capable of producing sustained hypertension, but without in any way compressing the renal pedicle.

tial hypertension. The significant difference between this type of experimental hypertension and the human malignant variety is that in the former no characteristic changes are found in the glomeruli and arterioles of the ischemic kidneys. These changes are thought to be the result of hypertension and the action of some chemical substance. The clamp protects the kidney from the hypertension, which presumably is not the case in man

It was found, however, that when one ureter was occluded and the main renal artery of the opposite kidney markedly constricted, hypertension, renal insufficiency, and uremia resulted (Goldblatt and Kahn, 1940). Under these circumstances the renal arterioles of the kidney with unobstructed blood supply but occluded ureter showed the characteristic pathological changes seen in both intrarenal and extrarenal arterioles in the malignant phase of essential hypertension in man. These changes were not present in the kidney with the obstructed main renal artery, again indicating that hypertension within the renal vessels is necessary for the production of typical pathological changes. At the present time it would appear that renal insufficiency to the point of uremia is a necessary factor in the production of intrarenal lesions in animals comparable to those seen in man. While the pathological changes may be identical, certainly uremia, or even serious impairment of renal function, as judged by ordinary tests, is not necessary for the production of this phase of essential hypertension in man.

The effect of interruption of sympathetic pathways on experimental renal hypertension has been studied by several investigators. Denervation of the renal pedicle (Page and Heuer, 1935*A*; and Collins, 1936) and even transplantation of one kidney with removal of the other to insure completeness of the sympathectomy (Blalock and Levy, 1937; and Glenn, Child, and Heuer, 1937) do not alter the hypertension. Cutting the splanchnic nerves with excision of the lower four thoracic ganglia was ineffective, as was section of the anterior spinal nerve roots from the sixth dorsal to the second lumbar inclusive (Goldblatt, Gross, and Hanzal, 1937; and Goldblatt and Wartman, 1937). Removal of the entire sympathetic nervous system in the thorax and abdomen including that innervating the heart neither prevented nor cured the hypertension (Freeman and Page, 1937).

named "angiotonin" (Page and Helmer, 1940). A similar substance, hypertensin, has been described by Muños, Braun-Menendez, Fasciolo, and Leloir (1940).

Besides renin and angiotonin, it would appear that antipressor substances are also formed in the body. These are capable of inactivating the pressor mechanism. In animals, both nephrectomy and the production of experimental renal hypertension enhance the pressor action of angiotonin. This effect is reduced, however, by large transfusions of normal blood. Other evidence of the presence of inhibitor substance has been discussed by Page (1940*A*). Williams, Harrison, and Grollman (1940) demonstrated that renal extracts reduce increased arterial pressure and act as an antipressor substance. The same authors (Grollman, Williams, and Harrison, 1940) reported a renal tissue extract which was effective in lowering blood pressure in hypertensive patients when administered orally. A similar effect was reported by Page, Helmer, Kohlstaedt, Fouts, Kempf, and Corcoran (1940), who injected renal tissue extract and found it to lower blood pressure for short periods of time in both hypertensive patients and animals. Also Page, Helmer, Kohlstaedt, Fouts, and Kempf (1941) found administration of renal tissue extract to cause a significant fall in blood pressure and treated eleven patients in this manner for short periods of time. Certain untoward effects were thought to be due to impurities.

Merrill, Williams, and Harrison (1938) observed that injections of renin cause decreased renal blood flow and increased renal volume. The increased renal volume is attributed to constriction of glomerular efferent arterioles. Corcoran and Page (1940*A*) have also studied the effect of renin upon the kidney. Slow infusion of this substance in dogs increases the proportion of water removed from plasma by glomerular filtration. The increase in the proportion of water removed from the plasma must result from increased intraglomerular pressure and, in association with decreased renal blood flow, must occur as the result of efferent arteriolar vasoconstriction. The intensity of the renal vasoconstriction does not parallel the degree of elevation of arterial pressure. This suggests inequality of the distribution in the body of the vasoconstriction caused by renin, which is emphasized by the observation of Landis, Montgomery,

Hypertension resulted when either one or both kidneys were so treated, being more intense as a rule in the latter case. If only one kidney was involved, removal of this organ or the cellophane wrapper resulted in a return of the blood pressure to normal. Preliminary denervation of the renal pedicle did not prevent the development of hypertension.

Humoral Mechanism. It seems quite clear that a humoral agent is elaborated by the kidney when its blood supply is altered in a significant manner. This acts upon the peripheral arterioles, causing increased resistance to blood flow and hypertension. In the past few years a great deal of investigative effort has been expended in clarifying this matter.

In 1898 Tigerstedt and Bergmann discovered that extracts of kidneys contain a protein which causes prolonged rise in arterial pressure when injected intravenously. This substance they called renin. Until recently little more was known about it. At present it appears that renin alone is not a vasoconstrictor, but combines with an "activator" to form angiotonin, which is *thought to be the true vasoconstrictor. Page, Corcoran,* Helmer, Fouts, Kohlstaedt, and Kempf have written in detail concerning humoral mediators of hypertension and have developed methods of purifying renal extracts (Helmer and Page, 1939). They noted that the more active the extracts became in elevating arterial pressure in intact animals, the less vasoconstriction they caused when perfused with Ringer's solution through an isolated organ such as the rabbit's ear. Apparently something had been lost during purification which was necessary for the vasoconstrictor action of renin.

They reached the conclusion that renin alone was not a true pressor substance. When blood, or a pseudoglobulin fraction of blood, was added to purified renin its vasoconstrictor action in isolated organs could be restored (Kohlstaedt, Page, and Helmer, 1940), although the effect on arterial pressure of intact animals was not affected. It would appear that the proteins discarded in the purification of renin contained an "activator" which was necessary for the vasoconstrictor action of renin. The prolonged time required for the interaction of renin and renin-activator *in vitro,* suggested that the reaction was enzymatic. The product of this reaction has been isolated, crystallized, and

Character of the Change in Renal Blood Flow Responsible for Elaboration of Renin. Kohlstaedt and Page (1940) have investigated this matter because they found that moderate hypertension in dogs could be produced by compression of the renal artery without clear evidence of reduced renal blood flow. They therefore questioned the term renal ischemia, which implies a markedly reduced arterial supply to the kidney. They found that in perfusion experiments involving a dog's kidney, as the renal artery was constricted, the mean arterial pressure and blood flow distal to the clamp could be maintained at nearly their former normal physiological levels by increasing the stroke volume of the pump. The pulse pressure in the renal artery distal to the clamp, however, was reduced by about 50 per cent. Samples of renal venous blood taken during perfusion with oxygenated blood without constriction and before application of the clamp showed no evidence of the presence of renin. Samples taken about an hour after application of the clamp showed large and increasing amounts. They concluded that the stimulus to renal hypertension is reduction of pulse pressure, not necessarily accompanied by reduced blood flow, within the kidney.

Renal Blood Flow in Man. In contrast to the obvious pathological changes in the peripheral arteries of hypertensive individuals, evidence of impaired renal flow or of primary vascular disease within the kidney is often absent or negligible when judged by the ordinary clinical tests of renal function. As a result the possibility that the kidney is the primary source of trouble has not seemed reasonable. Moreover, extrarenal (heart, brain) causes of death in this disease are approximately four times as frequent as renal failure. But at autopsy, with the exception of the spleen, the kidney is actually found to be the most frequent site of vascular disease and its arterioles show the most marked changes. The careful, thorough, and accurate methods of studying renal function in normal and hypertensive individuals which have been developed by Smith and co-workers (1938 and 1939) are very important. Their publications constitute a thorough review of past knowledge and present concepts, and should be studied by all interested in this matter. By means of inulin, diadrast, and phenol red clearances they have established means of estimating the function of the glomeruli and tubules separately. They also can quantitate renal blood flow in

and Sparkman (1938) that the pressor action of renin, unlike that of adrenin or pitressin, occurs without a fall of skin temperature. Since cutaneous temperatures are not decreased in hypertension, this characteristic of renin is also a necessary property of the pressor substance of essential hypertension.

Infusion of angiotonin, the effector substance of the action of renin, causes nearly the same changes in renal blood flow, glomerular filtration and arteriolar pressure as does renin. Corcoran and Page (1940*B*) believe that the differences in the action of renin and angiotonin lie in the rapidity and intensity of their effects and are those which would be expected from a pressor agent which, when presented as renin, is slowly liberated into the blood, and, when presented as angiotonin, is available for instant action. Similar qualitative identity and quantitative difference in the effects of renin and angiotonin on blood pressure and on renal and femoral arterial blood flow have been shown by other methods of measurement (Herrick, Corcoran, and Essex, 1941). The observation that femoral arterial blood flow may be increased while renal blood flow is decreased during the pressor action of angiotonin is in accord with the view that angiotonin may be the pressor agent of hypertension. Similar effects of angiotonin on renal blood flow, glomerular filtration, arterial pressure and cutaneous temperature have been obtained in studies on normotensive human beings (Corcoran, Kohlstaedt, and Page, 1941). The effects of angiotonin and its parent substance, renin, on the kidney and circulation parallel the circulatory alterations of hypertension in human beings; namely, increased arterial pressure without fall of skin temperature and decreased renal blood flow due to efferent arteriolar constriction.

Page (1940*B*) found renin to be liberated into the renal vein in increased amounts from the kidneys of hypertensive dogs, and Harrison, Blalock, and Mason (1936) found it increased in the renal parenchyma of hypertensive dogs. Both hypertensive patients and dogs show increased blood content of renin-activator and decreased concentration of inhibitor. According to Page (1940*C*), evidence is therefore accumulating which suggests that angiotonin, the pressor substance, which is the product of interaction of vaso-inactive renin and renin-activator, may be active in the production of experimental renal hypertension and essential hypertension in man.

upright position. On the other hand, pyrexia has a variable effect upon renal blood flow. Some patients show no increase of consequence, while others respond in a manner comparable to that of the normal person by doubling their renal blood flow under basal conditions.

It seems clear from these observations that a significant reduction in renal function and blood flow exists in the earliest stages of hypertension. These findings offer strong support to the concept that a causal relationship exists between perturbation of kidney function and hypertension. They appear to answer the objection to this concept which has been raised, owing to the fact that ordinary methods of detecting evidence of impaired kidney function used in the past almost invariably failed to indicate evidence of renal abnormality in the early stages of the disease. Armed with these accurate and quantitative methods of study it should be possible to determine the effect of interruption of vasomotor pathways to the kidney and splanchnic bed upon the renal contribution to hypertension. Perhaps, in time, such studies will cast further light upon the mechanism which initiates the alteration of renal function in the earliest stages of this disease.

Influence of Endocrine Factors on Experimental Hypertension of Renal Origin. Certain endocrine glands appear to play a rôle in the complicated mechanism whereby hypertension results from experimental renal ischemia. Removal of the pituitary gland in animals with established hypertension causes it to be reduced or abolished. On the other hand, preliminary hypophysectomy will moderate but not prevent this type of hypertension (Page and Sweet, 1936 and 1937). The indirect rôle of the pituitary is not clearly understood. Loss of its pressor principle and its stimulating action upon the adrenal cortex have both been suggested as possible factors.

Bilateral adrenalectomy both abolishes established hypertension and prevents its development (Goldblatt, 1937*B*). Vigorous treatment with salt and cortical extract will result in elevated blood pressure in some animals. That the presence of some adrenal cortical tissue is necessary for the production of renal hypertension was shown by experiments in which one adrenal was removed, the medulla of the remaining gland destroyed, and the entire cortex or a small portion of it was left sufficient to main-

cubic centimeters per minute. This has enabled them to study renal circulation under basal conditions and to determine the effect of drugs, renal hyperemia, renal vasoconstriction induced by standing, and interruption of extrinsic renal innervation (spinal anesthesia) upon blood flow in normal and hypertensive individuals.

From these studies they find that under basal conditions (horizontal position) the normal human kidney functions at about 50 per cent of maximal capacity, and that all the individual nephric units are at work. When the extrinsic renal nerve supply is interrupted by spinal anesthesia, there is no significant change in renal blood flow or function, indicating that the autonomic nervous system exerts little if any control over renal blood flow under resting conditions. When, however, a stimulus is applied such as that resulting from a lumbar puncture, renal blood flow may be abruptly reduced. Assumption of the upright position is invariably accompanied by a significant lowering of renal blood flow. This is due to reflex constriction of the afferent renal arterioles. Injection of adrenine will also result in a diminished renal blood flow. This, however, is due to constriction of the efferent glomerular arteriole. Renal blood flow is increased by pyrexia and may become twice as great as under basal resting conditions. *From these observations it is apparent that man is supplied with neurogenic and humoral control over the renal circulation. This control is intermittent, not continuous. If called into play with sufficient frequency, it could result in a significant reduction of renal blood flow. It seems likely that this mechanism is more highly developed and is activated more frequently in some individuals.*

Smith and his associates have also studied the kidneys of hypertensive subjects, and while the data are not yet complete their tentative discussion is of interest. They found that under basal conditions there is invariably an ischemia in terms of absolute blood flow, and that there is early and progressive loss of tubular function, while glomerular function is unimpaired, at least in the earlier and milder forms of hypertension. This situation is brought about by constriction of the efferent glomerular arterioles.

As in normal individuals, renal blood flow can be further reduced by invoking vasoconstriction, such as by assuming the

Walker (1939) by progressive ligation of the cerebral arteries of a dog.

Finally, chronic hypertension has been produced by carotid sinus denervation and section of the aortic depressor nerve (Bacq, Brouha, and Heymans, 1934). This interrupts afferent impulses which normally buffer or depress the activity of the circulatory centers in the medulla and thereby allows unrestrained activity of vasoconstrictor, cardio-accelerator, and adrenine-secretory centers. Hypertension of three to four years' duration, somewhat variable in nature and reaching levels as high as 250 mm. of mercury, has been produced in this manner. When acute, this type of hypertension is abolished by total sympathectomy in dogs, but not in cats. Later Heymans (1938) showed that total sympathectomy in three stages caused a reduction in blood pressure to normal in one dog previously made hypertensive in this manner. Nowak (1940) produced chronic hypertension in ten dogs in this way, but Nowak and Walker (1939) found that preliminary total sympathectomy in two stages in one dog failed to prevent subsequent hypertension (160–170 mm.) when the moderator nerves were sectioned. Page (1940*A*), in commenting upon the apparent discrepancies in these reported results, raises the question whether cardiac denervation was complete. It would appear that further study of this mechanism is needed before a resemblance between this type of hypertension and human essential hypertension can be established. In particular, it would seem desirable to study both the acute and chronic forms of this type of experimental hypertension in the light of more recent knowledge of circulatory pressor substances and alteration of renal blood flow.

IV. Etiological Factors in Essential Hypertension in Man

The foregoing summary of investigative studies, necessarily brief and incomplete, serves to illustrate the complexity of this problem. It also emphasizes the fact that the cause of essential hypertension is unknown. The implication is clear that various factors are involved, not necessarily always to the same degree, although the net result of many different combinations of these factors may be identical. Most important seem to be primary vascular disease, sympathetic outflow from cerebral centers, normal endocrine activity, and the presence of an angiospastic

tain life (Goldblatt, Lynch, Hanzal, and Summerville, 1934, and Goldblatt, 1937*B*). In such animals blood pressure became elevated when the main renal arteries were constricted. It has been suggested that a normal state of blood vessel reactivity is dependent upon the adrenal cortical hormone. Lacking this, the vessels no longer respond to chemical pressor stimuli.

Thyro-parathyroidectomy, pancreatectomy, and gonadectomy do not prevent or cause significant persistent lowering of hypertension due to renal ischemia (Glenn and Lasher, 1938; and Katz, Friedman, Rodbard, and Weinstein, 1939).

III. Experimental Hypertension of Neurogenic Origin

Hypertension has been produced in animals by a number of methods which do not involve mechanical constriction of the renal arteries or parenchyma. Acute hypertension may be produced by injecting fluid under pressure into the cisterna magna. The resulting hypertension is probably related to anemia of the autonomic centers (Naunyn and Schreiber, 1881; and Cushing, 1901, 1902, and 1903). Perfusion of the brain stem with blood containing increased amounts of lactic acid will greatly increase arterial pressure for as long as two hours (Raab, 1931). Acute anemia of the cerebral circulation will provoke intense hypertension (Nowak and Samaan, 1935) in the dog. Acute hypertension produced in these ways is undoubtedly truly neurogenic and is the result of a generalized increase in vasoconstrictor activity. Grimson, Wilson, and Phemister (1937) found that acute hypertension produced by increased intracranial pressure was abolished by total sympathectomy. Freeman and Jeffers (1940) demonstrated that this could not be reduced by partial sympathectomy unless it resulted in complete denervation of the heart, both neural and humoral. They also corroborated the findings of Grimson, Wilson, and Phemister (1937).

Chronic hypertension has been produced by intracerebral injection of kaolin. This is followed by an inflammatory reaction and hydrocephalus (Griffith, Jeffers, and Sindaver, 1935, and Griffith and Roberts, 1938). This type of hypertension can also be prevented by total sympathectomy (Page, 1937). Few pathological changes of consequence were noted after fourteen months of hypertension induced by kaolin (Hamperl and Heller, 1934). Chronic hypertension has also been produced by Nowak and

arterioles of the ischemic kidney are much more sensitive to adrenine than are normal renal vessels. Whether renal blood flow may be increased after adequate sympathectomy has not been conclusively demonstrated.

V. Treatment of Essential Hypertension by Sympathectomy

According to Peet (1940) the possibility of a surgical approach to the problem of hypertension was suggested by Kraus to Brüning and published by the latter in 1923. The matter was further discussed by Danielopolu (1923) and Pende (1932). In 1930 Pieri (1927 and 1932) actually performed a unilateral splanchnic resection for hypertension. In the same year Adson approached the problem by laminectomy and anterior root section and later reported this technic (Adson and Brown, 1934). Craig (1934) reported a subdiaphragmatic exposure of the splanchnic nerves. Peet (1935*A*) reported his first series of cases in which splanchnicectomy was performed by a supradiaphragmatic approach, the technic of which now generally bears his name. This series was begun in November, 1933. Celiac ganglionectomy was later advocated by Crile and has been performed by him since 1936. His early experiences were reported in 1938*A*. Page and Heuer (1935*A*) reported that renal denervation alone had no effect upon the blood pressure level in one case of essential hypertension, and later (1935*B*) found the same to be true in several cases in which the hypertension was associated with chronic nephritis. Experience with these surgical procedures has been reported by others (Page and Heuer, 1937*A* and *B*; Page, 1938; and Davis and Barker, 1939). Some have been abandoned for various reasons (Allen and Adson, 1940). The technic of others has been altered. One of us (Smithwick, 1940) has had experience since 1935 with a number of these operations and recently suggested a combined supra- and infradiaphragmatic approach which has been used for over two years.

At the present time, four operations are in common use: supradiaphragmatic splanchnicectomy (Peet), the subdiaphragmatic approach (Adson, Craig, and co-workers), celiac ganglionectomy (Crile), and combined supra- and infradiaphragmatic exposure. All have a similar purpose. Each has its advantages and disadvantages. Peet (1935*B*); Freyberg and Peet (1937);

in hypertensive patients. The effect might be purely passive in nature, the result of relaxation of a large portion of the vascular bed. According to this concept blood pressure would be lowered throughout the body and as a consequence vascular disease might regress in the kidney as in the retinal arterioles, and perhaps lead in time to improvement in the renal hypertensive mechanism.

The fact that extensive sympathectomy may reduce hypertension in man, whereas it fails in the Goldblatt dog, may be connected with the higher development of the sympathetic nervous system in the human species which is necessitated by the upright posture. Therefore its ablation in man may be expected to result in a more significant vascular relaxation, particularly *when postural hypotension is present in the early weeks after* total splanchnicectomy.

While this mechanism may be important, it does not appear to be the sole explanation for lowering of blood pressure. It does not explain the fact that there may be no significant lowering of blood pressure in the horizontal position after radical splanchnicectomy sufficient to produce marked postural hypotension. As time goes on and the latter disappears, indicating decrease in vascular relaxation, the blood pressure in the horizontal position may fall steadily and reach normal or near normal levels in the course of months to one year after operation. We have found such to be the case in about half the patients who obtain significant lowering of blood pressure after sympathectomy. This explanation does not account for the fact that marked regression of eye-ground changes may follow operation when no significant change in blood pressure level is noted at any time. It would appear therefore that some other explanation for the effect of sympathectomy on blood pressure in man is necessary.

From our experience, we are convinced that better clinical results follow extensive rather than partial splanchnic denervation (Tables XV and XVII). The more complete operation obviously results in greater vascular relaxation, which may be due in part to a more thorough inhibition of adrenal medullary secretion. We know that all denervated vessels are more sensitive to adrenine than when normally innervated. Moreover, a recent report (Schroeder and Steele, 1940) indicates that the

3.4 per cent. An idea of the severity of hypertension is given by the summary of the preoperative eye-ground changes in 219 patients (Table XII).

TABLE XII. CLASSIFICATION OF SEVERITY OF HYPERTENSION IN PATIENTS REPORTED BY PEET, WOODS, AND BRADEN (1940) ON BASIS OF CHANGES IN EYE-GROUNDS

Abnormal Eye-Grounds		209
Group I	13	
Group II	50	
Group III	105	
Group IV	42	
Normal Eye-Grounds		10
Total		219

Less encouraging results in a small but very carefully studied group of patients followed this operation in the hands of Page and Heuer (1937A). We have employed this operation in a somewhat larger series of cases. Our results judged solely by the effect upon blood pressure are presented in Table XV. They are similar to those reported by Page and Heuer. Peet's results are not tabulated according to the four groups often utilized to indicate the severity of the disease. Hence it is impossible to discern the relative success obtained in the mild as contrasted with the more advanced stages, particularly as regards lowering of blood pressure.

In discussing selection of cases, Peet states that patients should preferably be below fifty years of age, and that renal function should be adequate as indicated by a urea clearance over 40 per cent of normal and a concentrating ability of at least 1.012. The non-protein nitrogen should not exceed 45 mg. per cent. The heart should be compensated. Little information is given regarding preoperative tests or findings which might indicate that a favorable blood pressure response could be expected, other than stating that the prognosis is more favorable in females than males, and also in the age group below thirty. He believes that operation has improved life expectancy, as more than half of 95 cases operated upon five years or more ago are alive. He also believes that no other form of therapy, medical or surgical, has been reported which offers as good results in patients suffering from hypertension of an equal degree of severity.

Adson and Allen (1936); Allen and Adson (1938 and 1940); Craig (1939); Craig and Adson (1939); Crile (1937, 1938*A* and *B*, and 1939); and Peet, Woods, and Braden (1940) have made a number of reports of progress in recent years. The latest available statistics of each will be summarized and discussed in terms of our own experiences.

Supradiaphragmatic Splanchnicectomy. Peet, Woods, and Braden (1940) have recently summarized the results in 350 consecutive cases upon which Peet has operated in the past seven years. This constitutes the largest series by one surgeon, using the same technic in every case, and with the longest follow-up which has yet been reported. Of these 350 cases, 290 have been followed from nine months to seven years. The findings are summarized in Table XI. As performed by Peet, this operation consists of a one-stage procedure in which the lower three dorsal ganglia and intervening trunk, together with as long a segment of the great splanchnic nerve as can be obtained through an eleventh rib exposure, are removed on both sides.

TABLE XI RESULTS IN 290 PATIENTS TREATED BY SUPRADIAPHRAGMATIC SPLANCHNICECTOMY FOR HYPERTENSION, REPORTED BY PEET, WOODS, AND BRADEN (1940)

(Patients followed postoperatively from 9 months to 7 years.)

Blood Pressure	Reduced to normal { not over 130/90 up to age 30; not over 150/100 after age 40 }	11.7%
	Markedly reduced (at least 80/25)	7.6%
	Significantly reduced (at least 40/15)	51.4%
General Disability	Symptoms improved	86.6%
	Complete recovery incapacitation	55.5%
	Total cases with improvement incapacitation	81.3%
Eye-Grounds	Disappearance papilledema when present	73.8%
	Total cases with improvement	69.4%
Heart	Heart size diminished	64.0%
	Electrocardiogram improved	53.4%
Renal Function	Urea clearance improved	52.2%
	Urine concentration improved	44.8%

Many tables are presented which give details of the preoperative and postoperative findings with regard to symptoms, blood pressure, eye-ground changes, heart, and kidney findings. In addition, they are given for each postoperative year. The percentage of improvement and lack of improvement are surprisingly constant per postoperative year, indicating that the results are persistent and not temporary. The operative mortality was

pressure falls below 140/100 in response to rest, the chances of a worth-while result are about 50 per cent. If the resting level is 140–180/100–110 a favorable response may be expected in about 25 per cent. If the resting range is 180–220/110, a satisfactory response will result in only 6 to 7 per cent of the cases. When the maximal preoperative diastolic pressure was 115 or less, a favorable response to operation resulted in over 50 per cent of the cases. This figure was reduced to approximately 25 per cent when the diastolic level exceeded 115. They also found that when the diastolic level fell below 100 in response to sodium amytal sedation (3 grs. every hour for three doses), a satisfactory outcome followed in about 30 per cent of the cases, but if the level exceeded 100, the effect of operation was almost invariably unsatisfactory.

As a result of their experiences Allen and Adson find that the circumstances which indicate a poor result are inadequate response of blood pressure to rest, advanced hypertension (Group IV), and advanced arterial disease as exemplified by marked sclerosis of the retinal arteries. They believe it is useless to operate on patients who have congestive heart failure, auricular fibrillation, angina pectoris, significant renal insufficiency, or severe hypertensive encephalopathy.

Celiac Ganglionectomy. This operation as performed by Crile (1937, 1938*A* and *B*) consists of excising both celiac ganglia with division of the major and minor splanchnic nerves. It is done in two stages. In a period of approximately three years, 357 celiac ganglionectomies were performed for relief of essential hypertension in 213 patients. In one series of 175 celiac ganglionectomies (number of patients not stated) there were 5 deaths, a mortality per operation of 2.8 per cent. As of October, 1939, 123 operations have been performed without a death. The effect upon the blood pressure of 61 cases followed for three or more years is given (Table XIV).

Crile finds that the calendar age is not as important as physiological age. He does not believe that reduction in blood pressure should be the sole measure for judging the effect of operation as a form of treatment of hypertension. He feels that the effect upon the eye-grounds, cardiac and renal function, and symptoms should also be considered. He finds that cerebral deterioration and impaired renal function (urea clearance below 50 per cent)

Subdiaphragmatic Splanchnicectomy. A recent discussion of 300 cases operated upon during the past five years is reported by Allen and Adson (1940) of the Mayo Clinic. A two-stage operation was performed in each case. There were no operative deaths. The splanchnic bed was denervated by subdiaphragmatic resection of the splanchnic nerves, including a portion of the celiac ganglia and the upper two lumbar ganglia. Cases operated upon within six months of the time of writing were excluded. The observation period of the 224 cases summarized was from three months to five years (Table XIII). Good results include cases with normal maximal systolic and diastolic pressures, some with normal systolic and slightly elevated diastolic, a few having mild elevation of both systolic and diastolic, and a number with elevated systolic but normal diastolic pressures. There are no cases in the fair result group with strictly normal systolic and diastolic pressures. Most of the patients have mild to moderate elevations of systolic and diastolic levels, a few having near normal systolic with elevated diastolic, and several having elevated systolic and normal diastolic pressures.

TABLE XIII. RESULTS IN 224 PATIENTS TREATED BY SUBDIAPHRAGMATIC SPLANCHNICECTOMY FOR HYPERTENSION REPORTED BY ALLEN AND ADSON (1940)

EFFECT UPON BLOOD PRESSURE

(Patients followed postoperatively from 3 months to 5 years)

Good	*Fair*	*Temporary or Poor*
27 (13%)	41 (18%)	156 (69%)

Group	*No. Cases*	*Good and Fair*	*Temporary and Poor*
1	11 (5%)	45%	55%
2	137 (61%)	35%	67%
3	69 (31%)	26%	74%
4	7 (3%)	0	100%

EFFECT UPON SYMPTOMS (% Relieved)

Effect upon Blood Pressure	*Headache*	*Dizziness*	*Tiredness*	*Thoracic Pain*	*Shortness of Breath*
Good and Fair	94	90	56	72	65
Temporary and Poor	79	92	60	59	54

A real attempt has been made to determine the value of observations and tests in the selection of patients who are most likely to benefit by operation. It appears that if the blood

TABLE XV. EFFECT OF SUPRADIAPHRAGMATIC SPLANCHNICECTOMY ON BLOOD PRESSURE IN 66 PATIENTS OPERATED UPON IN THE MASSACHUSETTS GENERAL HOSPITAL

(Cases followed 3 months to 4½ years.)

	No. Cases	*Significant Effect*	*No Significant Effect*
Group I	13	5	8
Group II	19	1	18
Group III	17	0	17
Group IV	17	0	17
Total	66	6 (9.1%)	60 (90.9%)

In Table XV, as in other tables showing our results, the cases are arranged according to eye-ground changes. In Group I there is arteriolar constriction only, whereas in Group II there is tortuosity and nicking of veins at crossings. Patients in Group III have more marked arteriolar changes and have in addition associated retinitis, which is evidenced by hemorrhage or exudate or both. In Group IV are patients who have so-called malignant hypertension and are so classified because of the associated papilledema, usually with hemorrhage and exudate. None of the patients in Groups I and II (Table XV) had significant changes in renal function. One case in Group III and 5 in Group IV had marked impairment of renal function. The blood pressure was considered to be reduced in a significant manner if both systolic and diastolic pressure fell below 140/100, if either the systolic or diastolic level was normal, or if both were slightly elevated but materially reduced by comparison with the preoperative ranges.

A study of Table XV indicates that operation was more effective in Groups I and II. These contain the younger patients as a rule, with a predominance of females, and a milder degree of hypertension as judged by blood pressure ranges. Data bearing upon these points are given in Table XVI.

TABLE XVI. BLOOD PRESSURE RANGE, SEX AND AGE DISTRIBUTION OF 81 CASES OF HYPERTENSION GROUPED ACCORDING TO EYE-GROUND CHANGES (MASSACHUSETTS GENERAL HOSPITAL SERIES)

	Group I	*Group II*	*Group III*	*Group IV*
No. Cases	15	24	21	21
Average Preoperative Blood Pressure Range	203–166 / 130–110	229–183 / 142–115	236–189 / 147–122	256–206 / 164–132
Sex	F-M/7-1	F-M/4-1	Equal	Equal
Age	29	39	40	37

TABLE XIV. RESULTS IN 61 PATIENTS TREATED BY CELIAC GANGLIONECTOMY FOR HYPERTENSION REPORTED BY CRILE

(Patients followed postoperatively 3 or more years.)

Pressure Reduced	*Systolic %*	*Diastolic %*
20 points or more	78.6	57.1
30 points or more	57.0	35.7
40 points or more	42 9	14 3
50 points or more	21.4	7.1
75 points or more	7.1	——

Average Age	*% Living*	*Average Preop. Blood Pressure*	*Average Postop. Blood Pressure*	*Symptomatic Relief*	*Now Working*
46	55	213/130	187/115	88%	82%

are contraindications to operation. He believes that celiac ganglionectomy has increased the life expectancy of these patients. This may be due, in part, to improvement of cardiac function which is implied by the finding that among those dying after operation, heart disease is much less frequently the cause of death (11.8 per cent) than in unoperated cases (60 per cent). The technic of this operation is commented upon in Chapter XVII. It is our opinion that this is an unsound surgical procedure. Furthermore, we believe that celiac ganglionectomy (postganglionic sympathectomy) is unphysiological.

Summary of Personal Experiences. To the experiences of others we add a summary of our own. This has been rather varied and extends over a period of six years, during which time a number of different surgical measures have been applied to approximately 150 patients. At first a few cases were treated by bilateral subdiaphragmatic alcohol injection of the splanchnic bed, and by bilateral subdiaphragmatic splanchnic resection with excision of the upper lumbar sympathetic trunks. Unilateral or bilateral subtotal adrenalectomy was performed in 5 cases. In 1 case, the anterior roots were sectioned from T_6 to L_2 inclusive by Dr. W. J. Mixter. This varied experience comprised approximately 20 cases.

Supradiaphragmatic splanchnicectomy was performed in a series of 90 patients. There were 2 operative deaths. The early results in 66 cases are given in Table XV. Those too recent for analysis are deducted, as are those having known renal disease such as glomerular nephritis and pyelonephritis.

sure in the horizontal position after addition of bilateral lumbar sympathectomy.

These experiences led us to believe that splanchnicectomy should be performed by a combined supra- and infradiaphragmatic approach, completing each side in one stage. This can be carried out without difficulty if the twelfth rib is resected and the diaphragm divided from its lateral border inward to the crus, one inch below and parallel to the pleural reflection (see Chap. XVII). This operation interrupts vasoconstrictor impulses to the lower extremities, as well as to the entire splanchnic bed. Such a denervation is more complete than can be performed through an approach which is either entirely above or below the diaphragm and consequently greater vascular relaxation should follow. This effect may be an adequate explanation for the improved results as judged by more significant lowering of blood pressure in the horizontal position. However, it seems possible that the greater fall in blood pressure may be indirectly due, in part at least, to a more thorough interruption of pathways capable of causing reflex constriction of the afferent renal blood supply as well as secretion of adrenine. We have noted fibers to the renal plexus arising from L_1, and from the trunk between L_1 and L_2. A branch may arise from the second lumbar ganglion. We can therefore confirm the findings of Mitchell (1935), who has made such a careful study of the origin of the nerve supply to the splanchnic bed, the kidney, and the adrenal gland. Our present concept of the nerve supply to these areas is illustrated in Figure 58.

In a period of slightly over two years the combined thoracolumbar exposure has been used in 58 patients with hypertension. The majority of these have had essential or malignant hypertension, although some have had known organic renal disease. There were 2 deaths following the first stage of the operation. The results in those instances in which sufficient time has elapsed to evaluate the blood pressure response are given in Tables XVII and XVIII. While the number of cases is small, it seems as if this more complete denervation of the splanchnic bed has improved the results and decreased the percentage of insignficant responses in all stages of the disease. A favorable effect upon blood pressure in Groups III and IV has resulted for the first time in our experience. Examples of sig-

The results given in Table XV suggest that, as the effect of operation in apparently similar cases is not uniform, the question may properly be raised whether, because of anatomical variations, the same operation may fail to result in an effective denervation in some individuals. If this were the case and could be overcome, more uniform results in similar cases and perhaps better results in the more advanced groups might be expected. However, we realize that in even the earliest stages of the disease the different factors which cause hypertension may make one of two apparently identical cases less responsive to this form of treatment.

We elected to eliminate variations in the completeness of splanchnic denervation as far as possible. Accordingly, a few patients who had not responded to supradiaphragmatic splanchnicectomy were subjected to a further procedure, in which the first, second, and third lumbar ganglia were removed in two stages by a subdiaphragmatic extraperitoneal approach, making every attempt to extend the operation upward to the lower end of the previous field. Other cases were also denervated in four stages, again performing the supradiaphragmatic splanchnic resection first and the lumbar sympathectomy later, observing the effect of each procedure. In all of these patients the sympathetic trunk was removed from T_{10} to L_3 inclusive, and the great splanchnic nerves excised bilaterally over as long an extent as is possible through an eleventh rib exposure. In performing a supradiaphragmatic splanchnicectomy the intention is to remove the lowest three thoracic ganglia. The twelfth is often impossible to reach, and at times the ninth, tenth, and eleventh are probably removed instead. Likewise, the twelfth ganglion is quite difficult to reach with certainty from below the diaphragm; hence it is probable that in some cases the twelfth ganglion is not removed. In one case a "total" sympathectomy was performed in 7 stages, removing the sympathetic chains bilaterally from above the inferior cervical ganglion to below L_3.

As the splanchnic denervation became more complete, a significant fall in blood pressure was noted when the patient assumed the upright position. In our experience this is rarely observed after supradiaphragmatic splanchnicectomy alone. Some of the cases showing no response to supradiaphragmatic splanchnicectomy *maintained a significant fall in blood pres-*

TABLE XVII. EFFECT OF THORACOLUMBAR SYMPATHECTOMY ON BLOOD PRESSURE IN 26 CASES OF ESSENTIAL AND MALIGNANT HYPERTENSION (MASSACHUSETTS GENERAL HOSPITAL SERIES)

(Patients followed 4 months to 2 years)

	No. Cases	*Significant Effect*	*Effect Not Significant*
Group I	8	6	2
Group II	5	5	0
Group III	6	2	4
Group IV	7	4	3
Total	26	17 (65%)	9 (35%)

In addition to removing the great splanchnic nerves from the semilunar ganglion to the midthoracic level, the sympathetic trunks were excised from T_9 to L_1, inclusive, in all cases. In some L_2 was removed as well on one or both sides. Cases grouped according to eye-ground changes.

TABLE XVIII. EFFECT OF THORACOLUMBAR SYMPATHECTOMY ON BLOOD PRESSURE OF 8 HYPERTENSIVE PATIENTS HAVING KNOWN RENAL DISEASE (MASSACHUSETTS GENERAL HOSPITAL SERIES)

	No. Cases	*Significant Effect*	*Effect Not Significant*
Group I	1	0	1
Group II	2	0	2
Group III	3	1	2
Group IV	2	0	2
Total	8	1 (12.5%)	7 (87.5%)

The operations were similar to those performed in Table XVII. The cases are grou...
thre...
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areas which can be removed by combined lumbodorsal sympathectomy are indicated. We have drawn freely upon the findings of Mitchell (1935) and his dissections of stillborn babies. The usual origin of the great splanchnic nerve from T_5 to T_9 is indicated, as well as accessory fibers which may arise from the three ganglia above. Fibers running from the great splanchnic nerves to the aorta above the diaphragm are sh...

least splanchnic nerve arises from or just below T_{12} and terminates in the aorticorenal ganglion, or the intermesenteric or renal plexus. Other fibers to the renal plexus may arise from ...

G.S.	Great splanchnic nerve.	R.	Renal ganglion.
L.S.	Lesser splanchnic nerve.	R.A.	Renal artery.
Ls.	Least splanchnic nerve	R.P.	Renal plexus.
A.G.	Adrenal gland.	I.M.	Intermesenteric plexus.
S.G.	Semilunar ganglion.	Lum	Lumbar splanchnic nerve.
A.R.	Aorticorenal ganglion.	Inf	Inferior mesenteric plexus.

S.H.P. Superior hypogastric plexus.

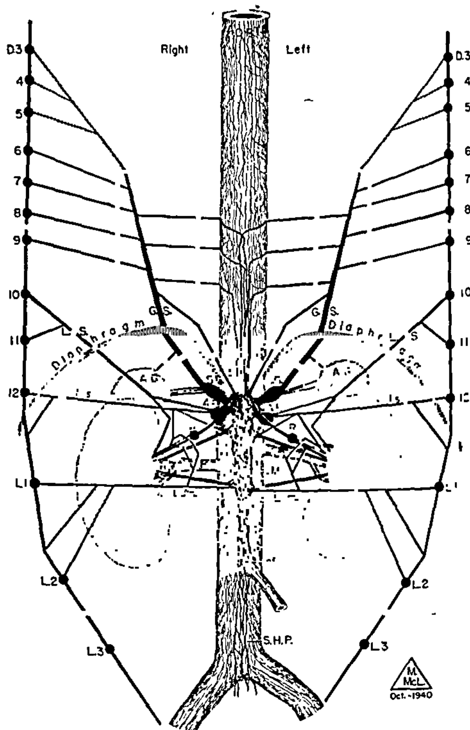


FIG 58. Sympathetic nerve supply of splanchnic bed, kidneys, and adrenal glands.

This diagrammatic representation of the nerve supply to the splanchnic bed is presented to indicate the widespread origin of the pathways concerned. The

return and increased pulse rate. If the upright posture is mair tained until syncope is imminent, a vasovagal reflex, presumabl mediated through the carotid sinus, may be initiated.

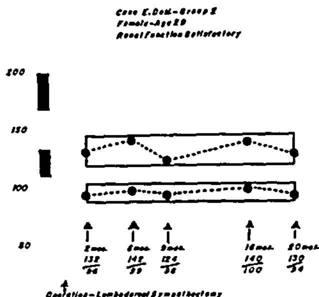


FIG. 60. Reduction of blood pressure following lumbodorsal splanchnicectomy for hypertension, Group II.

The black rectangles denote known variations in systolic and diastolic pressures before operation.

Recently MacLean and Allen (1940) have called attenti to the fact that sleeping with the head of the bed elevated inches eliminates the postural fall in blood pressure resulti from operation. This is associated with an increase of extr cellular fluid in the lower extremities which may prevent po ing of blood in the upright position. In one case, nonoperati an increase in whole blood volume of 410 cc. was noted after fo days of the above regime. This is of interest because of t known increase in plasma volume after total sympathectomy cats (Hamlin and Gregersen, 1939). Also, it is interesting to nc the significant postural changes in blood pressure described Lee and Freeman (1940) in their cases of angiomata of t lower extremities associated with varicose veins. Venous pooli appears to be a very important factor in postural hypotensic

Selection of Cases for Sympathectomy. It is apparent th the blood pressure of certain patients can be lowered in a s nificant manner by splanchnicectomy. That this is lasting a

nificant reduction of blood pressure levels after this operation in all stages of the disease are illustrated in Figures 59 to 63.

When the splanchnic bed has been thoroughly denervated, marked postural hypotension is produced. This is abrupt in

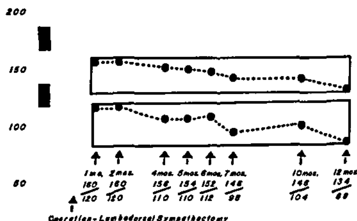


FIG 59. Reduction of blood pressure following lumbodorsal splanchnicectomy for hypertension. Group I

The black rectangles denote known variations in systolic and diastolic pressure before operation

appearance and profound in degree. The abruptness and severity lessen in a few weeks, are rarely severe after a few months, but may be present to some degree as long as two years after operation if the patient stands absolutely still for several minutes. In the early weeks after operation the fall in blood pressure on standing may be so extreme that the patient may be unable to remain upright. This profound postural change can be overcome by bandaging the legs from the instep to knee and by applying a snug abdominal binder beneath which a sponge rubber pad is placed to compress the lower abdomen. These may be gradually eliminated and are usually unnecessary after two or three months. Patients should be cautioned, however, not to stand absolutely still for long, but to move about slowly when in the upright position. At the first sign of faintness or dizziness the patient should either sit or lie down. Relief is then instantaneous. The most likely explanation of this phenomenon is relaxation of the venous bed, resulting in decreased cardiac

not temporary has been thoroughly demonstrated. Some of these patients may be cured of their disease. For others, the clock appears to have been turned back several years at least. Significant lowering of blood pressure is almost invariably followed by improvement of symptoms and a favorable change in cerebral, cardiac, renal, and ocular manifestations if present before operation.

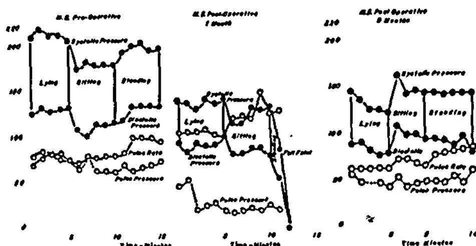


FIG. 63. Postural changes in blood pressure before and after lumbodorsal splanchnicectomy.

This is the same case illustrated in Figure 61. The abrupt fall in pressure on standing usually disappears in one to four months.

In the majority of instances, however, there has been no significant lowering of the blood pressure level. Many of these patients have obtained a high degree of symptomatic relief and have been able to return to work. In some, objective improvement as judged by favorable eye-ground changes has been noted. A few have derived symptomatic relief only. Occasionally no improvement of any sort resulted. Insufficient time has elapsed since operation to tell whether the life expectancy is favorably affected. All of these factors should be taken into consideration in judging the value of operation in the patients of this group.

It seems advisable to consider all factors which may be of value in predicting a favorable effect from operation. The best index is reduction of blood pressure. There is no rule which will cover all circumstances. Our purpose should be to eliminate those cases in which a poor result can be predicted with cer-

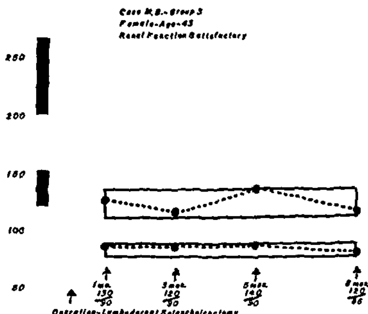


FIG. 61 Reduction of blood pressure following lumbodorsal splanchnicectomy for hypertension, Group III.

The black rectangles denote known variations in systolic and diastolic pressures before operation.

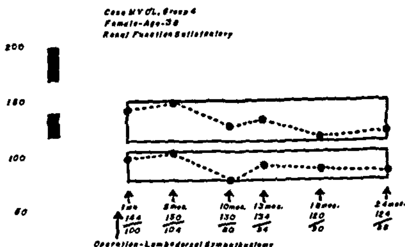


FIG. 62. Reduction of blood pressure following lumbodorsal splanchnicectomy for hypertension, Group IV.

The black rectangles denote known variations in systolic and diastolic pressures before operation.

The best results of sympathectomy are impressive. The mechanism by which blood pressure is lowered in man by sympathectomy is not completely understood. It may be due to a favorable effect upon factors which combine to reduce or alter renal blood flow, which in turn results in impairment of function and destruction of kidney tissue. It may be due to an extrarenal effect, such as vascular relaxation, either arterial or venous or both, or in part to inhibition of adrenal secretion. With the recent development of methods for detecting the humoral factor (angiotonin) in peripheral venous blood and for measuring renal blood flow it should be possible to obtain significant data on these important questions in the near future. At the present time great emphasis should be placed upon the selection of cases for sympathectomy, on further study of the mechanism whereby this results in persistent and significant lowering of blood pressure in certain cases, and upon determining how extensive the operation should be.

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tainty and to select those in whom a favorable effect can be foreseen with accuracy. There remains a small borderline group which it is difficult at the present time to be sure about.

From personal experience the matter might be summarized as follows: If the operation is adequate—and by that is meant bilateral excision of the sympathetic trunks from T_9 to at least L_1 inclusive, together with both great splanchnic nerves from the semilunar ganglia to the midthoracic level—a favorable result can be expected in nearly all Group I and Group II cases (Table XVII). Unfavorable results may be anticipated in these groups if renal function is impaired. This practically never occurs in Group I and II cases. An unfavorable result may also be suspected if the blood pressure range for the patient is excessively high for the group in question. This refers particularly to the lowest diastolic levels. Furthermore, the response is likely to be unfavorable if the blood pressure fails to fall to normal on sedation induced by administering 3 grains of sodium amytal every hour for three doses. Groups III and IV contain the more advanced cases (Table XVII). Even in these excellent results may be obtained if renal function is still satisfactory (when the kidneys are capable of concentrating urine to a specific gravity of 1.020 or better and excreting above 20 per cent phenolsulphonephthalein in the first fifteen minutes). As in the case of Groups I and II, an unusually high blood pressure level which fails to drop to normal on sedation, coupled with reduced renal function, tends to indicate a poor result. These are unfavorable signs even in the presence of good renal function. More important, however, are other evidences of advanced vascular changes, such as cerebral accidents and particularly impaired cardiac function. These, combined with poor renal function, almost certainly indicate an unfavorable result. The fact that an occasional brilliant result may follow splanchnicectomy even when impaired renal function exists should not be overlooked. Examples of this have been reported by Peet (1940). Such results are usually accompanied by improvement of renal function. They might be anticipated if one could demonstrate beforehand when renal function can be favorably altered. To date this has been impossible. The presence of known renal disease (Table XVIII) is an unfavorable sign, mild hydronephrosis being a possible exception.

The best results of sympathectomy are impressive. The mechanism by which blood pressure is lowered in man by sympathectomy is not completely understood. It may be due to a favorable effect upon factors which combine to reduce or alter renal blood flow, which in turn results in impairment of function and destruction of kidney tissue. It may be due to an extrarenal effect, such as vascular relaxation, either arterial or venous or both, or in part to inhibition of adrenal secretion. With the recent development of methods for detecting the humoral factor (angiotonin) in peripheral venous blood and for measuring renal blood flow it should be possible to obtain significant data on these important questions in the near future. At the present time great emphasis should be placed upon the selection of cases for sympathectomy, on further study of the mechanism whereby this results in persistent and significant lowering of blood pressure in certain cases, and upon determining how extensive the operation should be.

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Chapter XIII

THE LUNG

It has been shown in Chapter III that the anterior and posterior pulmonary plexuses receive their extrinsic innervation from the vagi and from the inferior cervical and upper four thoracic sympathetic ganglia. For the details of the neuroanatomy of the lung the reader should examine Figure 13, which is reproduced from Braeucker (1927), and read the outstanding contributions of this investigator (1926*A* and *B*, 1933). Each lung receives a bilateral as well as a bisystem supply. Fontaine and Herrmann (1928) have carried out complete extrinsic denervation of the lungs in dogs, but conclude that an active intrinsic control remains, which is mediated by a large number of ganglion cells in the bronchial walls. This is comparable to the intrinsic plexuses of the intestine and prevents a complete functional denervation.

Phillips and Scott (1929) and also Rienhoff and Gay (1938) have given clear descriptions of the nervous control of the human bronchial musculature and the secretion of its mucous glands. Apparently the vagus carries constrictor fibers to the trachea and larger bronchioles, for Weber (1914) observed that stimulation of the distal end of the nerve resulted in constriction of the main bronchi and its paralysis in dilatation. A striking roentgenographic demonstration of this effect has been published by Francis (1929). It has been confirmed in man by Tucker (quoted by Kern, 1926), who observed a definite unilateral limitation in bronchial constriction through the bronchoscope after section of the left vagus. Dixon and Ransom (1912) claimed that stimulation of the upper thoracic sympathetic ganglia in animals commonly resulted in bronchodilatation on one or both sides. By the use of more refined methods Braeucker, as well as DeBurgh Daly and von Euler (1932), found that

stimulation of either the vagus or the sympathetic nerves in the dog might cause an increased resistance to the interchange of air. This has been confirmed by Binger, Gaarde, and Markowitz (1930), who demonstrated reflex bronchoconstriction persisting in curarized guinea-pigs after paralysis of both vagi. Very recently Hebb (1940) has reported that stimulation of the stellate ganglion produces marked bronchoconstriction in the isolated perfused lung of the guinea-pig. It would appear from her experiments that this bronchoconstrictor effect results from a cholinergic discharge and is of the same order as that produced by stimulation of the peripheral ends of the cut cervical vagi.

In an investigation of bronchomotor reflexes, Dixon and Ransom (1912) found that bronchoconstriction could be elicited by stimulating the central end of one vagus or the thoracic sympathetic chain. A constrictor reflex was never obtained after section of both vagi. These facts suggest that sensory neurons which are known to run in the vagal and sympathetic pulmonary rami (Møllgaard, 1912) may form the afferent half of a bronchoconstrictor reflex arc whose efferent fibers lie in the vagus. This is theoretically most attractive, but cannot be relied on, as these experiments have never been confirmed. The whole question of the innervation of the bronchioles must therefore remain *sub judice*. The difficulty here, as in the case of the gastrointestinal innervation, probably lies in the intermingling of parasympathetic and sympathetic axons in the thoracic vagi and the sympathetic ganglia, as well as in the relative autonomy of the intrinsic ganglia of the lung.

I. Bronchial Asthma

In attempting to relieve the paroxysms of dyspnea which characterize bronchial asthma through operations on the extrinsic pulmonary nerves, it must be admitted that theory rather than fact has been the basis from which this therapy originated. As stated by Alexander (1933), we do not know whether the asthmatic paroxysm is "due to spasm of the bronchial muscles, to edema of the bronchial mucosa, or to hypersecretion of the bronchial glands." Alexander presented evidence that all three factors play a part and that each is activated by vagal stimula-

tion. Viewed from this angle, destruction of the sympathetic pathways appears to be an unreasonable procedure.

In the group of asthmas due to sensitization to foreign protein, the onset of the attacks is most likely caused by a humoral mechanism. These patients constitute the class which obtain the greatest relief from medical therapy. There is, however, a growing realization that a large number of asthmatics cannot be explained on this basis. In these reflex spasm of the bronchi may play an important rôle. Some evidence for this rests on observations that psychic and emotional stimuli often lead to attacks. In the face of this nearly complete lack of scientific data, the fact that a certain small group of severe asthmatics fail to respond to any form of medical treatment has led surgeons to attempt their cure.

Kümmell (1923 and 1927) was the first to report surgical relief of bronchial asthma following a unilateral sympathectomy. Although he believed that the principal bronchoconstrictor fibers ran in the vagi, he felt that a sufficient quantity might be interrupted in the sympathetic trunk to diminish bronchial spasm. Following Kümmell's optimistic report many German, Russian, and French surgeons hastened to remove various parts of the cervicothoracic sympathetic system. Many of the early case reports present such inadequate data and such a brief period of observation after operation that they are of little value.* The best accounts of these operations have been published by Göbell (1928) and Leriche and Fontaine (1939) (Table XIX). In the majority of these cases operation was limited to a partial sympathetic denervation of one or both lungs. Since the most reliable evidence points to the vagus as the transmitter of bronchoconstrictor impulses, one is at a loss to explain the not infrequent accounts of benefit after sympathectomy, unless this is due to the interruption of the afferent limb of the reflex arc. Furthermore, from recent anatomical evidence that the main sympathetic control of the bronchi is transmitted over rami from the second, third, and fourth thoracic ganglia, it is difficult to comprehend how such a limited opera-

* In a critical evaluation of this work Dr. F. M. Rackemann, head of the [illegible] to have benefited.

tion as stellectomy can affect the bronchial tree in any way. A possible explanation of these difficulties is the fact pointed out by CoTui, Burstein, and Wright (1936) that the bronchioles become additionally sensitive to adrenaline after degeneration of their postganglionic sympathetic neurons, and that this increased bronchodilator response occurs when the stellate ganglia alone have been removed. Perhaps the denervated bronchioles become sufficiently sensitized, so that the patient's own circulating adrenaline can produce the favorable response.

Sympathetic denervation of a lung has been carried out by one of us (White) in 4 patients which were studied in collaboration with Dr. F. M. Rackemann. The denervation was performed by removing the upper thoracic sympathetic ganglia through a posterior approach in 3 patients and by paravertebral alcohol injection in the fourth. Ultimate results in these cases have not been impressive, and on account of them we have not planned further intervention along these lines.

Paravertebral injections of procaine and alcohol, which have proved so valuable in the control of cardiac pain, have been used in an attempt to interrupt all the pulmonary sympathetic rami. When such injections are made against the anterolateral aspect of the vertebrae, the chemical block may include the vagal fibers as well as the sympathetic. Stern and Spivacke (1930) were the first to apply this method to a case of bronchial asthma, but their injection failed to produce any striking results. DuBose (1931) claims to have observed complete relief in several cases a year after injection, but the description of his cases is too meager to be really convincing. In Baltimore, Dr. Benjamin Baker (personal communication) has carried out 16 bilateral alcohol injections of the upper five thoracic ganglia. He writes that in several the results were immediate and brilliant; in the majority the relief was great but not complete; and in 3 there was no effect whatever. All of these patients, however, suffered recurrences within two to six months and reinjection failed to benefit them. In view of its transitory results and the additional objection that alcoholic injections are often followed by a disagreeable neuritis, this method has little to recommend it.

From the modern physiological viewpoint bilateral resection of the vagal connections with the posterior pulmonary plexus would appear to be the most promising method of interrupting

TABLE XIX. A SUMMARY OF THE NEUROSURGICAL OPERATIONS WHICH HAVE BEEN PERFORMED FOR BRONCHIAL ASTHMA

Reporter	*Date*	*Total Cases*	*Total Operations*	*Operation*	*Number*	*Cured, Per Cent*	*Improved, Per Cent*	*Unimproved, Per Cent*	*Unknown, Per Cent*	*Mortality, Per Cent*	*Interval*
Göbell *	1928	98	105	Single sympathectomy	7	0	—	100	—	—	Uncertain; earliest operation 4½ years ago
				Double sympathectomy	19	42	11	42	5	—	
				Right vagotomy	1	0	—	100	—	—	
				One side sympathectomy plus vagotomy	16	50	—	19	31	—	
				Double sympathectomy with vagotomy	61	43	18	23	14	2	
				Total (by cases)	98	43	13	29	14	1	
Hesse *	1926	18	23	Unilateral sympathectomy, bilateral sympathectomy	18	28	16	56	—	—	Usually a year or so
Kaess *	1925	28	28	Unilateral sympathectomy	28	29	29	42	—	—	Over 6 months
Fründ *	1928	48	55	Sympathectomy	1	—	—	100	—	—	Not given; earliest case of 3 years' duration
				Vagotomy	47	13	21	66	—	—	
				Vagotomy and sympathectomy	7	—	—	100			
				Total (by cases)	48	12	21	67			
Lengemann *	1925	27	44	Unilateral sympathectomy	10	20	30	50	—	—	At least several months
				Bilateral sympathectomy	2	50	50	—	—	—	
				Vagotomy	3	33	—	67	—	—	
				Combined	12	33	33	26	—	8	
				Total (by cases)	27	33	26	37	—	4	
	1928	20	25	Unilateral sympathectomy	11	18	—	82	—	—	Over 2½ years
				Vagotomy	2	—	—	100	—	—	
				Bilateral sympathectomy	2	50	—	50			
				Combined	10	10	20	70	—	—	
				Total (by cases)	20	15	15	70			
				Total five series	211	30	18	44	7	1	
Leriche and Fontaine	1939	12	17	Bilateral stellectomy	14	50	50	—	—	—	2½ to 7½ years
				Unilateral stellectomy	8	12½	25	62½			1 to 13 years
Rienhoff and Gay	1938	10	20	Bilateral resection posterior pulmonary plexus	—	40	40	10	10	—	Over 2 years

* From article by Phillips and Scott, 1929.

bronchospasm of neurogenic origin. This operation was first performed by Phillips and Scott (1929). It has been given a thorough trial by Rienhoff and Gay (1938), who have performed a bilateral resection of the posterior pulmonary plexus in 10 severe asthmatics. In this operation a certain number of sympathetic rami must be divided in addition to all the vagal connections. When the results were reported two years after the last operation, 4 remained free of attacks and had been able to return to work; 4 more had occasional mild attacks of asthma, all of which were amenable to control by medication; 1, who had improved for three months, had then succumbed to cardiac failure; and only 1 had shown no improvement.

We have had but a single experience and in that patient only a unilateral denervation was performed. Its unsuccessful result cannot fairly be held against the method, since it is known that there is some bilateral innervation of each lung.

In summarizing the work that has been done on bronchial asthma, it appears that sufficiently radical resections of both the sympathetic and vagal pulmonary rami have now been performed to give a fair indication of the value of these operations. In the face of their inconsistent results, it does not seem possible to recommend sympathectomy for the treatment of this condition. On the other hand, total resection of the pulmonary vagal branches has some valid physiological backing. The results of Rienhoff and Gay are impressive and deserve continued study and a much wider trial. We should recommend that as a preliminary to operation the effect on vital capacity of a deep bilateral paravertebral injection with procaine should be determined.

II. Control of Pain in Pulmonary Disease

Swetlow (1926) has recommended the use of paravertebral alcohol injection for the relief of intractable pain from pleural irritation in pulmonary tuberculosis and other diseases. In experiences at the Massachusetts General Hospital with 3 cases of intractable pain due to carcinomatous involvement of the pleura, paravertebral alcohol block has been found to be inadequate. The reason for this is that the lung itself is nearly insensitive, and that pain occurs only when the parietal pleura is involved. This means that we are dealing not with visceral, but with so-

matic pain transmitted over the intercostal nerves. In all cases relief from injection was complete as long as these latter nerves were paralyzed, but recurred at the end of a month as they recovered. It has been emphasized in Chapter XI that intercostal paralysis from alcohol is of short duration, although the interruption of the delicate sympathetic rami is usually permanent.

In our experience pain from carcinoma of the apical pleura is one of the most difficult conditions which the neurosurgeon is called upon to relieve. In the superior pulmonary sulcus syndrome described by Pancoast (1932) the nerves at the base of the neck have been infiltrated by the growth, resulting in severe pain in the shoulder and arm, a Horner's sign, and in addition often a hoarse voice and reduced movement of the diaphragm from paralysis of the recurrent laryngeal and phrenic nerves. Under these circumstances it is necessary to perform a very high section of the spinothalamic tract. For painful conditions of the lower thoracic pleura, however, posterior root section is a satisfactory operation.

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Chapter XIV

GASTROINTESTINAL TRACT

I. Nervous Control of the Gastrointestinal Tract

It has been pointed out in Chapter IV that the antagonistic action between the sympathetic and parasympathetic divisions of the autonomic nervous system, which regulates other forms of visceral activity, is less clear-cut in the digestive tract. The essential mechanism that controls digestion lies in the intrinsic plexuses of the gastrointestinal canal. For this reason neurosurgical methods have failed to relieve such clinical conditions as hyperacidity and pylorospasm. There is, however, evidence to show that the activity of the digestive tract is reduced during periods of intense emotion, when there is a generalized outburst of sympathetic impulses. It is of interest to recall that Lister (1858) was one of the first to bring out the inhibiting action of the sympathetic system on peristalsis, which he demonstrated by passing an electric current through the lower thoracic spine and observing that with a certain strength of current "the 'hemmung' action came into play and the intestines became relaxed and motionless." Lister records that he "found the best mode of proceeding was to remove the skin and two layers of muscles from the abdomen of a rabbit, leaving the peritoneum and one layer of muscles, which are quite transparent enough to enable you to see any movements of the intestines, without the complication that the action of the air upon them involves."

There is much more physiological evidence than was formerly realized in favor of an antagonistic action of the thoracolumbar and craniosacral system in the control of the digestive processes. For example, when the sympathetic centers in the hypothalamus are stimulated there is a reduction in gastric tone and increased secretion of mucus, whereas when the anterior parasympathetic areas are excited there is a tendency to increased secretion of

acid (Heslop, 1938, and Sheehan, 1940). If the thoracic vagi are cut, food passes through the lower segment of the esophagus with such difficulty that a condition similar to human cardiospasm is produced in the cat and monkey (Knight, 1934, and Ferguson, 1936).* Similarly, when the "nervi erigentes," which carry the pelvic parasympathetic impulses to the rectum and lower colon, are paralyzed, a condition similar to human megacolon is produced in the experimental animal (Adamson and Aird, 1932). Ivy (1938) has summarized further observations which point in the same direction. For example, the sympathomimetic drugs ephedrine and benzedrine delay gastric emptying, whereas the parasympathetic stimulant "mecholyl" accelerates; insulin increases gastric motility by raising vagal tone, and this response is abolished by atropine.

Following his experimental production of cardiospasm in the vagectomized cat and its relief by sympathectomy, Knight (1935) and Knight and Adamson (1935) have submitted 3 cases of achalasia of the esophagus with cardiospasm to sympathetic denervation, resecting the left gastric artery and vein with the plexus of nerves that innervate the region of the cardiac sphincter. These operations and the result in a similar case reported by Meade (1939) were fairly successful. Fifteen other cases have recently been collected by Ochsner and DeBakey (1940). Although in some of these a less effective denervation was performed, the results on the whole are not impressive and further experience is essential before any definite evaluation of the method can be made. In selecting cases for operation emphasis must be given to Knight's statement that true cardiospasm and achalasia must be differentiated from hypertrophic stenosis of the cardia. This last group stands in the same relation to the former as does hypertrophic pyloric stenosis to pylorospasm. These conditions are separate entities and in cases of hypertrophic stenosis no good can result from denervation.

In the treatment of other abnormal conditions of the upper portion of the gastrointestinal tract surgical application based on experimental data has not been as effective as might have been expected. To reduce gastric secretion, Pieri and Tanferna (1930) cut the vagus nerves, either above or below the diaphragm, in 8 patients. They found a reduction of acid values postoperatively, but in the course of a few months these returned to normal. In corroboration of their findings, Hartzell (1929) observed in dogs that when the entire vagal supply was sectioned in the thorax there was a marked reduction of free and combined acid. Psychic secretion of gastric juice was entirely eliminated. However, when Vanzant (1931) re-examined Hartzell's dogs two years later, he found acid curves which were practically as high as before operation, although at autopsy he found no evidence of nerve regeneration. There are three possible explanations for these failures: (1) A high degree of automaticity of the digestive process, so that it can be regulated effectively by the intramural plexuses. (2) The mixed composition of the splanchnic and vagal trunks, with each containing fibers of both systems. The finding that a much purer response can be obtained on stimulating the respective centers in the hypothalamus than from either the thoracic vagus or splanchnic fibers is strong evidence for this. (3) The fact that both the splanchnic trunks and the vagi, which contain preganglionic axons, have such an extraordinary power of regeneration. Cannon (personal communication) believes that vagal cardioinhibitor fibers may again hook up with the heart even after the intrathoracic portion of the vagus has been transplanted into a new position outside the ribs.

Experimental attempts to modify the flow of bile from the gall-bladder have been equally unsuccessful, because the emptying of this reservoir is largely under the control of a humoral mechanism (Hillyard, 1930). This is also true of the external secretion of the pancreas, which is only partly under control of the autonomic nerves (see p. 94). So far as its internal secretion is concerned, attempts have been made by de Takáts and Cuthbert (1933) to control the hyperglycemia of diabetes by splanchnic and adrenal denervation, but these efforts have not been successful.

As regards the nervous control of defecation, there is evidence

that stimulation of the lumbar colonic nerves leads to contraction of the sphincter ani internus and relaxation of the detrusor muscle of the colon in the dog (Learmonth and Markowitz, 1929 and 1930). But from data obtained in a well planned investigation of defecation in man, Denny-Brown and Robertson (1935) have concluded that the mechanism which controls evacuation of the bowel is mediated entirely through the lower sacral segments of the spinal cord and its peripheral plexuses. There is no evidence that the sympathetic supply (superior hypogastric plexus) plays any part in these automatic reflex responses. After studying the activity of the large bowel in different lesions of the nervous system, White, Verlot, and Ehrentheil (1940) found that the smooth muscle of the rectum and colon reacts to distention in a manner quite similar to skeletal muscle after a sudden stretch; in other words, the peristaltic rush waves which sweep the contents of the colon down into the rectum are a form of stretch reflex and correspond to the reactions which have been so thoroughly studied in the bladder (see Chap. XV). As such they respond after injury in much the same manner as the reflexes of skeletal muscle. This evidence was obtained by recording the pressure curve during slow filling of the colon with warm water. When so recorded the colonmetrogram closely resembles the cystometrogram, except that the colon holds a three to four times greater volume of fluid. From a study of the changes in bowel activity after lesions at various levels of the nervous system it is clear that reflex activity and the ability to empty the colon effectively persist until the reflex centers in the sacral cord, the cauda equina roots, or the pelvic nerves have been injured. Determinations of intracolonic pressure-volume relationships (unpublished data) were also made before and after bilateral lumbar ganglionectomy and combined lumbar ganglionectomy and splanchnicectomy in a number of subjects with normal bowel function.* After sympathetic denervation of the normal rectum and colon no alteration was visible either in the basic tone of the bowel, its peristaltic activity, or its sensory acuity. Unfortunately it cannot yet be stated whether any change can be made out after sympathectomy for congenital megacolon, as we have had no opportunity to determine this important point. But in any event clinical evidence is incon-

* Patients with Raynaud's disease and essential hypertension.

trovertible that the ability of the dilated and hypertrophied large intestine to evacuate itself is greatly improved after removal of its sympathetic nerve supply.

The value of sympathetic denervation of the colon in children with Hirschsprung's disease has become so generally recognized that the older methods of colonic resection are falling into disrepute. Mortality in the latter group is formidably high and, as de Takáts and Biggs (1938) point out, a progressive dilatation of the segment proximal to the resection has been reported too often to be ignored.

The first form of surgical intervention for the neurogenic type of megacolon consisted of lumbar ramisectomy. This was proposed by Wade and Royle (1927), who observed a striking improvement in bowel activity in cases operated upon for spastic paraplegia. In the light of present day knowledge the second and third lumbar ganglia must be removed in order to prevent regeneration, and the operation is best performed through a posterior approach in two stages (see p. 424). Inasmuch as the colon is developed as a midline organ it is probable that the innervation of its right and left halves is derived from both sides, and it is better for this reason to resect the chain on the right as well as on the left. Adson (1937) and Leriche (1937*A*) have recommended cutting the splanchnic chains in addition to including the first lumbar ganglia in the resection of the lumbar chains.* Nerve fibers to the colon and rectum undoubtedly pass through the first lumbar ganglia, but since there is no evidence that splanchnic fibers reach the lower colon, there is no logical reason for including these structures unless the cecum and ascending colon are severely involved.

An operation which interrupts the colonic sympathetic fibers more specifically and leaves vasomotor control of the lower extremities intact has been developed by Rankin and Learmonth (1930). This consists of resection of the inferior mesenteric and superior hypogastric plexuses; the operation is carried out through a midline abdominal incision, and the preaortic sympathetic nerves are resected from the origin of the inferior mes-

* This procedure, as is the case with resection of the hypogastric nerves, causes sterility in the male (see p. 96), because the fibers which pass through the first lumbar ganglia stimulate peristalsis in the vasa deferentia and ejaculation. We therefore feel that this upper pair of ganglia should be preserved in the male, although it is best to include it in the resection in females.

enteric artery to a point 3 cm. below the aortic bifurcation (see p. 429). This procedure has the advantage of permitting intraperitoneal exploration, and of simultaneously influencing dilatation of the bladder and ureters when this condition is also present (Pässler, 1938). Its disadvantages are sterilization of the male and also the added risk of an intraperitoneal operation when the patient is poorly nourished. In our experience it has proved difficult to do a thorough denervation of the plexus around the inferior mesenteric artery. For this reason it is best to resect the left lumbar chain of ganglia at the same time, although this can also be carried out at a later date through a retroperitoneal incision if the patient fails to show a satisfactory improvement.

As regards indications for sympathectomy in patients with megacolon, we believe that operation should be performed only in children with the congenital form of the disease described by Hirschsprung (1887) who are not relieved by conservative medical treatment by the age of 5 or 6, although in some severe cases it will not be possible to defer operation to this age. It is obviously of the greatest importance to select for operation only such cases of megacolon as are of neurogenic origin. Scott and Morton (1930) have shown that these can be differentiated from other types by observing the effect of spinal anesthesia on the motility of the colon. Figure 64A shows the appearance of the

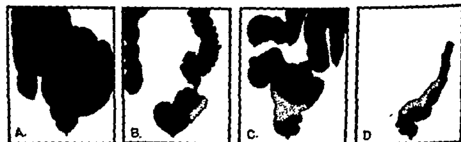


FIG 64. Barium enema in Case 1 with megacolon.

The x-ray films were traced on transparent paper and the areas filled with barium marked in black The stippled areas represent gas pockets.

A. Enlarged colon still full of barium after attempt at evacuation.

B. The degree of evacuation after spinal anesthesia In addition to its improved ability to empty, the colon shows active segmental peristalsis

C. Barium enemas repeated after sympathectomy. The colon is smaller and there is active peristalsis.

D. After expulsion of enema: A satisfactory ability to empty the colon has been restored.

colon after a barium enema and attempts at spontaneous evacuation. Spinal subarachnoid block was then induced with 100 mgm. of procaine crystals dissolved in 3 cc. of spinal fluid. As anesthesia rose to the nipples, active peristalsis swept over the colon and resulted in a copious bowel movement (Fig. 64B). After operation the patient showed a continued ability to empty the colon to a similar satisfactory extent (Fig. 64C, D). The therapeutic use of repeated lumbar subarachnoid injections of procaine has been advocated by Scott (1936) and by Telford and Simmons (1939), who have demonstrated that in many young children normal bowel function may be restored without the need of surgical denervation. Its failure in Case 3 below was due solely to lack of cooperation on the part of the patient's father.

In the cases where spinal anesthesia is followed by prolonged improvement in evacuation, recent evidence suggests that further benefit may result from treatment with parasympathetic drugs. We have not yet had an opportunity to test their action, but a recent paper by Law (1940) describes very encouraging results from the use of acetyl-beta-methylcholine bromide, accompanied by such simple auxiliary aids as liquid petrolatum and an occasional enema until the evacuation habit is established. This drug can be given by mouth, and its prolonged peristaltic action with minimal toxic effects makes it more effective than the other acetylcholine derivatives which have long been known to stimulate intestinal action. Law recommends an initial dose of acetyl-beta-methylcholine bromide of 0.1 gm. administered a half-hour after breakfast and increased after three days to 0.2 gm. If necessary it may later be increased by giving a similar dose in mid-afternoon. Overdosage is indicated by diarrhea. When the dosage is found which produces one to two stools a day the patient is discharged, usually taking 0.2 gm. of the drug each morning and from 1 to 2 tablespoons of the liquid petrolatum each evening, with instructions to use an enema in the event of constipation or distention. In Law's experience in the treatment of 6 children suffering from megacolon with acetyl-beta-methylcholine bromide and liquid petrolatum the results were entirely successful. It is therefore recommended that this form of medical treatment be given a thorough trial before operation is considered, and also that it be used post-

operatively in patients who fail to obtain an entirely satisfactory response after sympathetic denervation of the colon.

The postoperative course of carefully selected cases of Hirschsprung's disease should show a rapid improvement in the ability to defecate. The first postoperative enema is usually expelled with a force in striking contrast to those administered previously. By the time the patient is ready to get out of bed, spontaneous defecation has usually been established. With an intelligent patient who is willing to make serious efforts to evacuate the bowels, operation should result in a complete cure. On the other hand, *it must be remembered that defecation is not a passive process* and that all that can be expected from removing the inhibitor nerves is to place the rectum under the most favorable circumstances for carrying out its function. When the patient is uncooperative or still worse, as is often the case, feebleminded, operation should rarely be undertaken.

In the acquired type of constipation which fails to respond to medical measures, operation is useless. Here there is no reason to believe that the extrinsic innervation of the colon is directly at fault.

The most extensive tabulations of results of sympathetic denervation in congenital megacolon are to be found in the article by Ross (1935) and in Pässler's monograph (1938). According to the latter, of 117 patients reported in medical journals, 38 were fully relieved, 64 improved, 12 were failures, and 3 died. As the children's service at the Massachusetts General Hospital is relatively small, we have had a rather limited experience. Protocols of three typical cases follow:

Case 1. Doris B., 20, M.G.H #321489. Since the age of 14, this young woman had required cathartics or enemata in order to obtain a bowel movement. At 18 she came to the *Massachusetts General* Hospital diagnostic clinic, where x-rays were taken and showed idiopathic dilatation of her colon. Following this she was treated by a low residue diet and mineral oil. In this way she was able to move her bowels once to twice a week, but was constantly troubled by belching and flatus. In addition she complained of intermittent pain in her right flank, transient dizziness, and a constant sense of fatigue.

Physical examination revealed a sallow, poorly developed young woman with a very protuberant and tympanitic abdomen.

6/24/32: A spinal anesthesia test (Fig. 64) showed that the enormously dilated colon could empty itself to a surprising degree after the inhibiting action of the sympathetic nerves was removed.

6/28/32: Resection of the presacral and inferior mesenteric plexuses (as recommended by Rankin and Learmonth—see p. 429).

This operation resulted in better evacuation after enemata, but failed to produce spontaneous defecation. For this reason her left lumbar ganglia were resected by the posterior extraperitoneal approach on 8/9/32. A barium enema on the thirteenth day after operation showed the colon empty and considerably reduced in size. From the time she was first able to get up until her last visit to the follow-up clinic on 12/31/32 she had daily spontaneous bowel movements, but it has been impossible to obtain more recent information.

Case 2. Rose L., 14, M.G.H. #320450. This mentally retarded girl presented a history and physical findings practically identical with those in the preceding case. Her symptoms dated over a three and one-half year period. Pain in her right flank had led to appendectomy in another hospital. The patient had intermittent attacks of vomiting and very severe constipation, for which she was treated by a soft bland diet, large doses of mineral oil and milk of magnesia, and enemata three times a week administered by the district nurse. In an attempt to perform a barium enema, five pints of solution filled only the distal half of her colon. On account of her mental retardation and poor ability to cooperate, it was impossible to do a spinal anesthesia test.

4/12/32: Resection of the presacral and inferior mesenteric plexuses. The patient made an uneventful convalescence, but her obstipation was not relieved. As in the preceding case, it was difficult to make certain that all the rami given off to the inferior mesenteric artery were cut. Failure to interrupt these nerves completely probably accounts for the poor results of this operation in both cases.

1/9/35: Left lumbar ganglionectomy through a posterior extraperitoneal incision. After this second operation there was a gradual improvement in her abilty to move her bowels. This improvement was slow, due to her mental retardation and poor ability to follow a strict medical régime, but at four months, and again at nine months after operation her parents wrote that her bowels were moving well.

At a further follow-up examination five years later she had ceased having spontaneous bowel movements, but responded well to enemata and had no abdominal distention. A barium enema showed a colon with active peristalsis and without much enlargement, although it was elongated in the region of the sigmoid and there were some redundant loops. The barium was thoroughly evacuated.

It was our opinion that due to mental retardation and unwillingness to make intelligent efforts to move her bowels this girl was developing an acquired form of megacolon. An ileo-sigmoidostomy was finally performed, but without further improvement in her constipation.

Case 3. George O'B., 10, M.G.H. #339442. A delicate and underdeveloped boy had suffered from obstinate constipation for years. His

mother was dead and his father incapable of giving him adequate attention and care. For months the father had noted that the boy had a poor appetite and a distended abdomen. He had small watery stools and frequently soiled his clothes. Prior to admission he often felt nauseated and occasionally vomited. He first entered the hospital on 8/22/34. On physical examination the rectum was found to be impacted with feces, and the entire abdomen distended with a doughy mass. A barium enema showed that this mass was a dilated colon crammed full of feces. The enlargement was mainly in the sigmoid, which was elongated into two dilated loops. Enemata were unsuccessful until the rectum was emptied under spinal anesthesia. Active peristalsis and defecation began at this time and continued under enemata administered on the ward. He was then discharged on a low residue diet.

The boy lived with his father and careful medical treatment in the home was impossible. As a result of neglect he again became distended with feces and began to vomit. After repeated enemata for eight days, laparotomy was performed on 12/26/34. A thorough exploration showed no organic pathology except an extraordinary redundancy and distention of the sigmoid colon. Both sympathetic chains including the second to fourth lumbar ganglia were then resected. Lumbar ganglionectomy was performed in preference to the inferior mesenteric and presacral denervation of Rankin and Learmonth, because it seemed inadvisable to interfere in any way with the innervation of the genital tract in a young boy.

The boy began to have spontaneous bowel movements on the fourth postoperative day and has continued to have one or more daily evacuations during the six years following his operation. He has, however, grown up to be a mental defective and at a recent examination in the gastrointestinal clinic it was found that he again had a large fecal impaction in his rectum This has been the cause of frequent watery bowel movements and occasional soiling, but he has never been troubled by recurrent abdominal distention or vomiting.

He was again admitted to the hospital in December, 1940, and his impacted sigmoid and rectum emptied by enemata. A subsequent barium examination showed a greatly dilated rectum and sigmoid. The remainder of the colon was only slightly enlarged. A plate taken after evacuation showed that the lower dilated portion of the colon still emptied poorly. A colonmetrogram disclosed a very atonic and dilated colon, which filled without reflex contractions or the usual sensations of fulness to a volume of 6,700 cc. (more than three times the normal capacity). When the test was repeated two hours after an injection of mecholyl a few definite peristaltic contractions were observed.

In spite of these discouraging tests the boy is clinically improved. He has never developed evidence of recurrent obstruction and now has a good appetite and is able to take part in games. Since the

thorough emptying of his colon on the ward and medication with mineral oil and acetyl-betamethylcholine bromide he has been passing two formed stools a day. But the mental retardation of the patient and his family prevents efficient cooperation, and without intelligent supervision it is certain that he will suffer from recurrent impaction and further distention of his lower colon.

Surgical experience in these 3 patients has not been satisfactory. It is now obvious that the first 2 patients did not have congenital megacolon, but an acquired form of constipation. It is known that this condition does not respond well to sympathectomy. The third patient probably represents a true case of megacolon, complicated by mental retardation. His response to lumbar ganglionectomy on the whole has been favorable, but retarded by inadequate care at home. Unfortunately we have had no experience with this operation in younger children, in whom the most striking results have been claimed. From the Children's Hospital, where many more of these cases are seen, Dr. T. H. Lanman reports that results after bilateral resection of the second, third, and fourth lumbar ganglia have been favorable, although their staff is not yet convinced that the improvement in bowel function will be permanent. Supplementing the operation with repeated dilatations of the anal sphincter has been an added help. Increasing efficiency in medical treatment has greatly reduced the need for surgical intervention, but when this fails sympathetic denervation should be performed only in typical cases of congenital megacolon in which the response to spinal anesthesia has indicated a favorable outcome. Even then it is doubtful whether normal intestinal activity can be maintained without continued intelligent postoperative care.

II. Alleviation of Pain from the Abdominal Viscera

The following evidence indicates that the sensory axons from the abdominal viscera run with the sympathetic nerves, primarily in the splanchnics: When these nerves are cut, Sheehan (1932) has found that the sensory endings (Pacinian corpuscles) in the mesentery undergo degeneration. Weiss and Davis (1928) and Jones (1938) have shown that when a swallowed balloon is distended at varying depths along the intestinal canal, pain is referred to characteristic areas of the abdominal wall. Such pain can be relieved by subcutaneous procaine infiltration, but if fur-

mother was dead and his father incapable of giving him adequate attention and care. For months the father had noted that the boy had a poor appetite and a distended abdomen. He had small watery stools and frequently soiled his clothes. Prior to admission he often felt nauseated and occasionally vomited. He first entered the hospital on 8/22/34. On physical examination the rectum was found to be impacted with feces, and the entire abdomen distended with a doughy mass. A barium enema showed that this mass was a dilated colon crammed full of feces. The enlargement was mainly in the sigmoid, which was elongated into two dilated loops. Enemata were unsuccessful until the rectum was emptied under spinal anesthesia. Active peristalsis and defecation began at this time and continued under enemata administered on the ward. He was then discharged on a low residue diet.

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In spite of these discouraging tests the boy is clinically improved. He has never developed evidence of recurrent obstruction and now has a good appetite and is able to take part in games. Since the

opiates in large doses to control emotional factors and a coin dent diarrhea. It is evident that she could have suffered fr pain referred to the uninjected right side, and that the gang on both sides should have been blocked.

In painful conditions of the stomach, Läwen (1923) has de onstrated that the sensory pathways enter the spinal cord in seventh and eighth thoracic segments. But true visceral p from the stomach is rare and when present is usually due extension of disease into the mesenteries and the nerve plexu in the posterior abdominal wall. Under such circumstances i questionable whether it can be relieved by splanchnicector We have had no experiences with intractable pain of gas origin, but one of us (Smithwick) has treated 6 patients w severe pain in the back (shoulder and arm, thorax, and cos vertebral areas) due to ulcers of the posterior wall of the d denum which had eroded into the pancreas. Direct surgical tervention on the ulcer was carried out in the majority of th but in 2 in whom hypertensive heart disease and angina pect contraindicated major surgery, pain was effectively relieved paravertebral alcohol injection against the sides of the fi sixth, and seventh thoracic vertebrae on the right side. This followed by freedom from gastric pain up to a fatal coron occlusion eleven months later in the first case, and for over ei months (to date) in the second.

Chronic intractable pain from the lower intestinal tract i rarity, but its amenability to sympathectomy is illustrated the following case history:

Sylvia H., Beth Israel #24906. This young woman had complai for several years of excruciatingly severe low abdominal pain wh came in waves, with severe constipation, increased peristalsis, vomiting. She had a very redundant colon with irritability and sp of the cecum and ascending colon. In this state she was unabl tolerate any enemas or fluid in the colon, as this precipitated agonizing attack of pain which lasted for hours and required l doses of opiates for relief. For this condition she had been subjecte a series of four laparotomies, but entirely without benefit.

To test the pathways of pain transmission paravertebral injec of her upper l[illegible] carried out by [illegible] lumbar verteb[illegible] enema was tol[illegible] without discomfort.

ther distention is produced the pain tends to spread out into new areas. With more extreme distention a deep, poorly localized sensation makes its appearance, which represents the true "splanchnic" type of pain originally described by Ross (1887). Adson (1935) and Leriche (1937*B*) have stimulated the major splanchnic nerve in the course of operation under local anesthesia, thereby producing severe but poorly localized pain. Bentley and Smithwick (1940) determined the exact amount of pressure required to elicit pain with the balloon at a certain point in the jejunum. This point having been established, the procedure was repeated after unilateral and bilateral splanchnicectomies. After a unilateral operation, pain could be appreciated only on the unoperated side of the midline, whereas after bilateral section no sensation could be detected by the patient even with more extreme distention. The sensation of nausea alone appears to traverse the vagi and then only in part, as Walton, Moore, and Graham (1931) found that the vomiting stimuli from peritonitis also run in the splanchnic nerves.

By employing paravertebral injections of procaine, as described by Läwen (1923), von Gaza (1924), and Alvarez (1931), it is possible to map out accurately the segments which transmit sensation in malignant and other painful conditions of the gastrointestinal tract (Table II, p. 141). The technic for this has been discussed in detail in Chapter VII.

Pain from the Gastrointestinal Tract. Pain from the esophagus may be transmitted over a varying number of sympathetic rami, of which those from the fifth and sixth pairs of thoracic ganglia are commonly claimed to be the most important. This is probably correct when the painful stimulus comes from the lower thoracic portion. These ganglia and their communicant rami were infiltrated with alcohol on the left side in a patient (B. M. #2438) who had had burning *substernal* pain of six months' duration, and frequent emesis of secretions which collected above the point of obstruction due to a carcinoma. For a month the substernal distress disappeared; vomiting of retained secretions was cut down from fifteen times a day to four or five, and the daily intake of morphine was reduced from an average of 8 grains to 1. During the second month, the terminal month of her life, the family physician wrote that it was difficult to evaluate the degree of relief, because of the necessity of using

previously her gall-bladder had been drained at another hospital, but attacks of right upper quadrant pain and vomiting had continued. There had been no attacks of fever or jaundice. On re-exploration Dr. Smithwick found her gall-bladder buried in adhesions. After cholecystectomy he was able to pass a probe down the common and cystic ducts into the duodenum.

A year later she was again admitted because of increasingly severe right upper quadrant pain, which had recurred in attacks during the past month. At this time there was a palpable tender liver and a slight elevation in the icteric index and Vandenbergh level of serum bilirubin without obvious jaundice. Dr. Smithwick was forced to re-explore the common duct. On probing with a 2 mm. dilator, an obstruction was met at the ampulla of Vater. The duodenum was then opened and the stenosed ampulla cut to permit the passage of larger dilators up to the 6 mm. size, but none larger than this could be slipped down the narrow common duct. The duct was then drained by a T-tube, whose lower branch was long enough to pass through the ampulla into the duodenum. After this operation the patient was discharged with the tube in place and draining bile into the abdominal dressing. As long as the bile escaped there was no pain, but it would return on clamping the tube and disappear again with its release.

After a few weeks the tube came out and the sinus closed. Thereupon the old pain soon recurred, so that by April she was having constant discomfort in the right upper quadrant, and occasional sharp attacks which were different from her old gall-bladder colic. At these times pain radiated into her right scapular region, neck, face, and occasionally down the right arm. There had been no fever, chills, or jaundice. In the absence of evidence of obstruction it was concluded that bile must be reaching the duodenum through the contracted ampulla, but under sufficient back-pressure to cause pain from compression of the biliary ducts. In view of the findings at her previous operation, it was evident that the difficulties and risk involved in obtaining a permanent dilatation of the stenosed ampulla would be far greater than an operation to relieve her pain. Evidence obtained from the animal experiments recorded above and from the patient with carcinoma of the liver indicated that resection of the right splanchnic nerves would give the necessary relief.

Accordingly, on 5/2/38 Dr. Smithwick resected the major and minor splanchnic nerves in addition to a short length of the sympathetic trunk through a posterior supradiaphragmatic approach on the right side. The patient was discharged on the tenth day after operation and has remained free of the longstanding symptoms of increased pressure in the biliary ducts.

Gastric Crises of Tabes. The vomiting which accompanies tabetic crises cannot be relieved by paralyzing the splanchnic segments with procaine (personal experience), and undoubtedly is transmitted over the vagi. Six years ago, when the first

10/10/39: Right sided splanchnicectomy and resection of the upper lumbar sympathetic ganglia was performed, following which she became free of pain on the right side.

10/23/39: A similar operation was performed on the left side.

Bilateral denervation has given a most satisfactory result, so that when the patient was examined three months later she was having normal bowel movements and experienced no unusual discomfort when her colon was completely filled in the course of a colonmetrogram. (Since operation was performed at an outside hospital no preoperative colonmetrogram had been made, but the postoperative test was normal.) *The motor function of her colon is normal and pain relief complete twenty months after operation.*

Pain from cancer of the intestinal tract is practically never amenable to treatment by intervention on the sympathetic nerves. The discomfort is usually due either to obstruction or to involvement of the mesentery and the somatic nerves in the lumbosacral plexuses. In the first type enterostomy or some type of short-circuiting operation is indicated; in the latter cordotomy is usually the procedure of choice.

Pain from the Liver and Biliary Passages. Moore and Singleton (1933) studied biliary pain in animals by injection of irritant solutions into the hepatic artery. They found that the great majority of afferent fibers pass up the right splanchnic nerve, but that in addition a few may be carried in the left splanchnic as well.

In a woman with metastatic carcinoma of the liver following radical mastectomy, the enlarged liver filled the entire right side of the abdomen and caused intense pain throughout this area. The patient happened to be hypersensitive to all opium derivatives, so that no relief was possible through medication. Paravertebral block with alcohol gave most satisfactory relief of pain during the terminal fortnight of her life. Injection in this case was made in all the right splanchnic segments (T_6–T_{11}) and caused very slight discomfort.

Animal experiments (Davis, Pollock, and Stone, 1932) have shown that gall-bladder pain is referred over the right major splanchnic nerve. Splanchnicectomy has now been successfully performed on a number of patients suffering from chronic biliary pain which was intractable to direct surgical attack (Craig, 1934). This is brought out in the following case history.

Helen S., 45, B.M. #88059. This patient entered the hospital in 1936 with a longstanding history of gall-bladder attacks. Five years

Abdominal Pain of Unknown Origin. Articles by Archibald (1928), Scrimger (1929), and Alvarez (1931) indicate that certain cases of obscure abdominal pain, where even exploratory laparotomy has failed to demonstrate the causative factor, can at times be relieved by dividing the sympathetic visceral nerves. The method of selecting these cases by diagnostic procaine block has been outlined in Chapter VII. This method has resulted in a number of brilliant results after all other forms of medical therapy and often numerous ill-advised abdominal operations have failed. The following is a case in point:

Phyllis B., 40, P.H. #24808. This emotionally highstrung woman developed stabbing attacks of right upper quadrant pain immediately after the sudden death of her husband. Her neurological and general examinations revealed no abnormality except a congenital malformation of the intervertebral disc between the ninth and tenth thoracic vertebrae. Removal of her gall-bladder by another surgeon had intensified the severity of her attacks, which became frequent and intolerably painful. Half-grain doses of morphine alone gave relief, and the patient was becoming addicted to the drug.

6/11/29: Injection of the ninth, tenth, and eleventh intercostal nerves with procaine in the posterior axillary line, followed by alcohol injection of the tenth. This injection gave freedom from the painful attacks for six months.

5/6/30: Paravertebral injection of T_{10} with procaine again caused the pain to disappear.

5/8/30: Resection of ninth and tenth thoracic ganglia and a long segment of the major splanchnic nerve (right). Drs. W. J. Mixter and J. C. White.

Following this operation the upper abdominal pain disappeared. For a few months she complained of milder attacks in her lower abdomen and groin, which recurred in 1933 for a short period after the death of her daughter in an airplane accident. These were never referred to the upper abdominal segments, where the visceral nerves had been cut. When last heard from six years later she was perfectly well.

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Hirschsprung's disease: Indications for and results obtained by sympathectomy. *Surgery*, 1937, I, 859–877.

edition of this book was written, it was believed that cutting the communicant rami to the major splanchnic nerve was often sufficient to control the abdominal crises of tabes and should be tried before recourse to cordotomy. But even if the mechanism of the painful crises could be interrupted by this procedure (which has never been proved), it would usually be impractical to section a sufficient number of rami. The same objection applies to posterior rhizotomy. Foerster (1927) has reported cutting many posterior roots and both vagi below the diaphragm without relief of pain, also the failure of splanchnicectomy and even of cordotomy in certain instances. But following the excellent articles of Kahn and Barney (1937) and Hyndman and Jarvis (1940), section of the spinothalamic tracts has justifiably become the procedure of choice for the relief of the lightning pains in tabetic crises. If the section is carried deep down into the anterior horn of gray matter, relief appears to be reasonably certain. In the past six years 3 patients with tabetic crises have been subjected to anterolateral cordotomy in this hospital. The results in 2 were excellent, but in the third analgesia (loss of pain perception) was not complete and the result therefore was unsatisfactory. The following is a typical example.

Peter M., 45, M.G.H #27159. The patient, an Italian waiter, had acquired a penile sore at the age of 18, but a diagnosis of syphilis had not been made prior to the onset of tabes dorsalis seventeen years later. In spite of intensive treatment from this time on he had suffered from attacks of nausea, vomiting, and excruciating left-sided abdominal pain for over ten years. He described the pain as a sense of fulness which became so intense that he felt as though his stomach would burst. This required large doses of morphine. At the time of his first admission he had typical clinical and serological tabes dorsalis and was addicted to morphine Two procaine-alcohol injections of his upper lumbar ganglia and left splanchnic nerves had been performed at previous admissions, but had resulted in only transitory relief of pain. On 10/18/34 his left splanchnic nerves were resected beneath the diaphragm, but this was no more successful than the injections.

1/26/35: Section of right spinothalamic tract by Dr. John S. Hodgson produced analgesia to the nipple line. The patient made a rapid convalescence and was discharged from the hospital free of pain twelve days later. He has been followed over the intervening years and has had no further tabetic pain. With freedom from pain he has also been relieved of morphine addiction and is able to work as a waiter in a large hotel.

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CHAPTER XV

INNERVATION OF THE UROGENITAL TRACT

KNOWLEDGE of the arrangement of the pelvic visceral plexuses is based on the painstaking dissections of the French anatomists Latarjet and Bonnet (1913), Hovelacque (1927), Elaut (1932), and Delmas and Laux (1933). The results of their studies have been summarized in Chapter III (see p. 90). Briefly summarized from the surgeon's viewpoint, the bladder, prostate, and seminal vesicles receive a mixed sympathetic and parasympathetic innervation through the hypogastric ganglia. These ganglia consist of a fine plexus of nerves which lie behind the trigone of the bladder. Their parasympathetic component is derived from the second, third, and at times fourth sacral segments over the pelvic autonomic rami (nervi erigentes) (Fig. 19). Their sympathetic fibers come from the lowest thoracic and highest lumbar segments of the cord and descend in the preaortic and presacral plexuses. In the original description by Latarjet and Bonnet (1913) the plexus at the aortic bifurcation was called the presacral nerve. Elaut (1932), however, has shown that it forms a single nerve trunk in only one case in four. In Hovelacque's terminology it is known as the superior hypogastric plexus. This is a more descriptive name, but the term presacral nerve has come into such common usage that it may be used as a synonym, provided it is understood that it refers to a variable plexus formation. A short distance below the sacral promontory the superior hypogastric plexus forms two paired trunks, the hypogastric nerves, which run to the corresponding terminal plexuses. From these a great number of delicate fibers are distributed to the pelvic viscera.

Physiology of Micturition. The function of the two systems of nerves to the bladder has been studied in both animals and man. An excellent review of the earlier work in this field was pub-

Ross, J. P. The results of sympathectomy: An analysis of the cases reported by Fellows of the Association of Surgeons. *Brit. J. Surg.*, 1935, XXIII, 433–443.

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Kolb, and Lewis (1940) believe that the responses of the bladder neck to sympathetic stimuli are entirely a sexual mechanism (part of the mechanism of ejaculation) and have nothing to do with micturition. In addition, they have been unable to detect any abnormalities in micturition after removal of the sympathetic nerve supply. We are prepared to accept this evidence and the work of Denny-Brown and Robertson (1933), and to reject the older theory that the sympathetic system favors the storage of urine and inhibits micturition.

The immediate effect of parasympathetic paralysis, as seen in injuries to the sacral segments of the spinal cord, the sacral roots, or their ventral extension as the pelvic nerves (nervi erigentes), is a flaccid paralysis of the bladder. This was first demonstrated by Elliott (1907), who found that destruction of the spinal cord at progressively lower levels did not destroy reflex evacuation of urine until the second, third, and fourth sacral segments were removed. Munro (1936) and McLellan (1939) have shown that *the resultant severely crippled bladder may gradually regain* some degree of function, but the type of emptying seen in the "atonic" (Fig. 65*A*) or "autonomous" (Fig. 65*B*) bladder is usually that of overflow distention, and an effective power to evacuate urine is never regained. The degree of impairment is far more profound in the totally insensitive bladder which may develop in tabes and in combined system disease (atonic bladder) than after lesions of the cauda equina (autonomous bladder). The reason for this probably depends on the retention of a vague sense of bladder filling in the autonomous bladder, which may reach the intact lower thoracic spinal segments through the afferent hypogastric fibers or in the lower intercostal supply to the parietal peritoneum.

Whereas injury to the spinal reflex centers in the second, third, and fourth sacral segments or their peripheral nerves results in severe degrees of paralysis, cystometric examinations have shown that lesions in the descending spinal tracts * and brain are followed (after a brief period of "spinal shock") by a permanently hyperirritable bladder which reacts to a small volume of fluid by precipitate urination. These states have been classified as

* Barrington (1933) has presented experimental evidence that the descending motor fibers to the bladder are located in the dorsal half of the lateral columns (pyramidal tracts).

lished by Fearnsides (1917). At first it was believed that the characteristic antagonistic action between the two divisions of the autonomic nervous system applied to the control of the bladder. Elliott (1907) may have been responsible for this error, as he found that in the cat "the hypogastric nerves facilitate retention of urine by constricting the sphincter and inhibiting the tone of the detrusor urinae." These conclusions drawn from the cat have been disproved by Evans' (1936) recent investigations on the same animal with more refined modern neurophysiological methods. After studying motor impulses over the two sets of nerves to the bladder with the Matthews oscillograph Evans concluded that "it has been impossible to obtain evidence of a satisfying nature that the sympathetic system plays any part in bladder activity." In a most impressive study on the human bladder, Denny-Brown and Robertson (1933) have demonstrated that urination is a reflex act mediated through centers in the sacral cord. Stretch of smooth muscle in the bladder wall sets off a detrusor reflex over the pelvic nerves, with contraction of the viscus and relaxation of its sphincters. Only after the intravesical pressure rises does the internal sphincter open. The external sphincter opens later, but it cannot be opened voluntarily. Its only voluntary power is the ability to contract and stop the flow of urine. This act is effected by somatic motor impulses over the internal pudendal nerve, whereas the afferent and efferent arcs of the detrusor reflex are carried over parasympathetic axons in the pelvic nerves. No evidence has been discovered that the sympathetic presacral fibers play any rôle beyond constricting blood vessels and contracting the bladder neck to an uncertain extent. Contraction of this region is associated with the muscular act of ejaculation (see p. 96), and this function is paralyzed by presacral neurectomy. This action has been confirmed by Learmonth (1931*A*) in a series of direct observations made on the operating table. On stimulating the presacral nerves contractions of the ureteral orifices, of the bladder trigone with its blood vessels, and of the internal sphincter were observed through a cystoscope. In addition to these effects, clouds of prostatic secretion and ejaculation of the contents of the seminal vesicles were seen in each of six observations. Whether there is a definite internal vesical sphincter which actually contracts in response to sympathetic stimuli is still a debated point. Langworthy,

recent monograph of Langworthy, Kolb, and Lewis (1940). After consideration of conclusions drawn from their own outstanding investigations and from many other sources, they deny the existence of any antagonistic action between the sympathetic and parasympathetic innervations of the bladder.

Effect of Sympathectomy on the Paralyzed Bladder. Six years ago, when the first edition of this book was written, the greater part of the work on the physiology of urination cited previously had not been reported. As a result of erroneous theories that the sympathetic fibers carried inhibitor impulses to the bladder, it was generally believed that certain cases of urinary retention due to cauda equina injury and disease could be improved by presacral neurectomy (Learmonth, 1932). Unfortunately these hopes have not been realized and this operation can no longer be regarded as a logical procedure (McLellan, 1939). The only condition in which there is evidence to suggest that sympathetic denervation may be of value in bladder dysfunction is the rare situation in which dilatation of the bladder is associated with congenital megacolon (Ross, 1935; Pässler, 1938).

The recent pharmacological discovery of potent parasympathomimetic drugs, such as the derivatives of acetylcholine and prostigmine, has held out the hope that medical therapy might be effective in the treatment of the severely paralyzed bladder. Unfortunately, this has not been the case. In this hospital the use of these drugs has been uniformly unsuccessful. Similar conclusions have been reached by Nesbit and Gordon (1941), who state that this form of therapy has "had no clinical beneficial effect in . . . any . . . type of neurogenic bladder." *

Afferent Innervation of the Bladder. Like all hollow viscera, the bladder is sensitive to overdistention and to spasmodic contraction, which give rise to painful sensations by stretching or squeezing its intramural nervous network. That the great majority of afferent nerves run in the parasympathetic trunks is proved by the fact that all painful sensation from the bladder and urethra is lost after section of the posterior sacral roots, injuries of the cauda equina, or the pelvic nerves. Apparently no

* Langworthy, Kolb, and Lewis (1940) do not entirely agree with this, as they have stated that beta-methylacetylcholine hydrochloride is of some value in the treatment of the tabetic bladder.

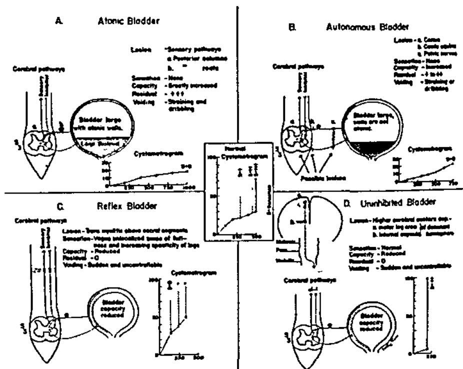


FIG 65. Classification of different forms of bladder paralysis.

This diagram follows the outline given in McLellan's monograph (1939). The distinction between the atonic and autonomous bladder would seem to be one of degree, rather than of fundamental difference in the nerve pathways involved. In each the reflex spinal arc is interrupted, and expulsion of urine must depend on the inefficient action of the intrinsic nerve plexuses of the bladder wall and passive compression by increasing intra-abdominal pressure. In the autonomous bladder the paralysis is less severe and atony less marked (possibly because a few nerve fibers remain intact).

In the cystometrograms given above the ordinates represent intravesical pressure in centimeters, the abscissae volume of filling in cubic centimeters.

the "reflex" (Fig. 65*C*) and "uninhibited" (Fig. 65*D*) types of paralyzed bladder. The action of the cerebral cortex is to inhibit reflex micturition (Langworthy and Kolb, 1933), and an inhibitor center appears to be located in the dominant hemisphere close to the leg area (Lewis, Langworthy, and Dees, 1935). In the baby and in some adult idiots cerebral voluntary control of micturition (as well as defecation) is not developed. Urine and feces are ejected at irregular intervals in response to the stretch reflex. With the gradual development of cortical function a cerebral control is established over these spinal reflexes. Its elimination results in increased reflex contractions of the smooth muscle which lines the bladder and rectum.

The best reference to the physiology of micturition is the

vesical spasm, in whom resection of the superior hypogastric plexus was followed by uniformly good results.

In our restricted experience, sympathetic denervation of the bladder by resection of the superior hypogastric plexus has a limited value in the treatment of intractable cystitis. The pain and frequency are usually not entirely relieved, but may be so reduced that urine can be retained over much longer periods in reasonable comfort. This is illustrated by brief case histories of two of the patients who have been submitted to presacral neurectomy.

Case 1. Mrs. Eva F., 39, B.M. #1768, was referred by Dr. E. L. Young. She had suffered from increasing irritability of the bladder and frequency for ten years. On admission her bladder had a maximum capacity of 60 cc. and she was forced to empty it every half hour because of sharp pain above the pubis. Numerous cystoscopies had shown an extensive area of scarring in the fundus, which cracked open easily. This had been fulgurated on numerous occasions. Urine examinations, including guinea-pig inoculation, had never shown tubercle bacilli.

12/1/30: Resection of the superior hypogastric plexus was performed, from which she made a good convalescence.

Following operation her bladder capacity remained about the same, but she noticed no more than a dull sense of discomfort above the pubis on distention. She was given a course of cystoscopic dilatations of the bladder by Dr. E. L. Young with further fulgurations of the ulcerated areas. These resulted in still further improvement. Three and a half years later Dr. Young reported that her original degree of improvement had been fully maintained.

Case 2. Mrs. Jessie McG., 50, B.M. #140453. This patient of Dr. J. V. Meigs had interstitial cystitis and a ventral hernia. Following a septic abortion twelve years previously, she began to suffer from dysuria and frequency. She had to get up three to four times a night and empty her bladder at hourly intervals during the day. Attempts to retain the urine for longer periods caused severe suprapubic pain. Physical examination was not remarkable except for diastasis recti and a large ventral hernia. On cystoscopy the bladder mucosa was found to be thickened and ulcerated; filling to over 90 cc. was intensely painful. The urine contained pus, but repeated tests for tubercle bacilli were negative, and there was no evidence of disease in the ureters and kidneys.

7/22/38: In addition to repairing the ventral hernia and removing the appendix, Dr. Meigs carried out a resection of the superior hypogastric plexus. The result was excellent. When examined seven months after operation she had no pain and had to get up only once a night to urinate; frequency was reduced to six or seven times during the day.

painful impulses traverse the sympathetic rami in the superior hypogastric plexus, because no diminution in sensation can be detected after presacral neurectomy, either on distending the bladder in the course of postoperative cystometrograms (Munro, 1937), or on testing its walls with tactile and thermal stimuli in the course of cystoscopy. Although Langworthy, Kolb, and Lewis (1940) believe that the vague sensation of bladder filling, which is present in many cases of cauda equina paralysis, is transmitted over afferent fibers in the hypogastric nerves, it is highly improbable that any sensation of actual pain is transmitted over this route.

Operations for the Relief of Intractable Bladder Pain. In spite of the evidence cited that the sympathetic nerves play no direct rôle in the transmission of pain from the bladder, case reports continue to emanate from well-known clinics recording relief by means of this operation. Pieri (1926) and Viannay (1927) were among the first to report favorable results of presacral neurectomy in the treatment of painful cystitis. Learmonth (1931*B*) stated that 4 of his 5 cases showed a degree of improvement which left no doubt that the operation was distinctly worth while, although none were completely relieved. Two years later Learmonth and Braasch (1933) had assembled 12 cases of painful cystitis treated by presacral neurectomy. Only one of these was due to tuberculosis. In a series of 11 cases, 8 of whom were suffering from tuberculous cystitis, Scott and Schroeder (1938) have reported an impressive degree of improvement in 9, considerable improvement in one other, and a single failure after six months of relief. Two of these patients required supplementary intrathecal injection of alcohol, in one to relieve residual burning in the urethra. These surgeons believe that better results can be obtained if the upper sacral sympathetic ganglia are resected with the superior hypogastric plexus. This is contrary to the opinion of Nesbit and McLellan (1939) and most other authorities.

According to Nesbit and McLellan (1939) it is possible that sympathectomy may relieve certain forms of bladder pain, not by interrupting afferent pathways, but by reducing spasm of the internal sphincter. In this interesting paper they describe a series of patients suffering from dysuria secondary to various forms of chronic cystitis with the predominating feature of

ply which differs from that of the kidney and bladder. Sympathetic rami run directly to the ureter from the lowest renal ganglia, the lumbar sympathetic chains, and the preaortic plexus. There are further connections between the ureteral nerves and the plexuses that supply the ovary and testes. Andler (1925) had previously shown that denervation of the ureter in animals does not disturb its peristalsis nor cause atony, dilatation, or stricture. Frommolt (1928) found that the ureter could be dissected out of its bed from the kidney pelvis to the bladder without impairing the rich anastomotic blood supply which enters it from both ends. The ureter, like the small intestine, can carry out its functions after total removal of its extrinsic nerves.

Wharton and Hughson (1931) reported 2 cases of intractable ureteral colic treated by denervation. Hepburn (1934) has reported 3 similar cases, and modified the operation to the extent of freeing the ureter over its entire length through a retroperitoneal incision and then displacing it as far laterally as possible, in order to prevent regeneration of its nerves. These cases had all shown persistent pain in the kidney region with evidence of irritation and spasm in the ureter on the insertion of a catheter. All occurred in women, and a theory has therefore been advanced that they were caused by reflexes from the closely related genital organs. Pyelography revealed no cause for the attacks other than ureteral spasm. Moreover, Peirson (in discussion of a paper by Stone, 1934) claimed that this pain is relieved by physostigmine, which diminishes ureteral tone, more effectively than by morphine. The results of denervation have been remarkably successful in each case reported.

A detailed anatomical study of the peripheral innervation of the kidney and ureter has been made by Mitchell (1935). Investigation of the spinal connections in the dog by White and Garrey (unpublished data) has shown that pain from distending the renal pelvis can no longer be felt after cutting the last thoracic, first and second lumbar posterior spinal nerve roots. It is highly probable that these are the important spinal segments in man, and that motor and sensory impulses reach the renal plexuses over the third or least splanchnic nerves and the gray rami from the first lumbar ganglia. Mitchell (1935) has described ganglia along the aorta near the origin of the renal arteries and a plexus of the fine rami running out along the renal

In contrast to the frequent favorable results in cases of chronic cystitis and irritability of the vesical trigone, little can be expected from resection of the presacral nerves in malignant involvement of the bladder. One such case (B.M. #7359), with carcinoma of the bladder developing at the site of an interstitial cystitis, obtained some relief from bladder pain, but no relief from the sense of burning and irritation in the posterior urethra. Rochet (1921) devised a method of resecting the hypogastric ganglia at the base of the bladder and thereby obtained a complete denervation. This procedure has been reported by Learmonth (1931*B*) in 2 cases. Although relief can be achieved when the disease has not infiltrated too far into the perivesical spaces, it carries a high rate of mortality and results in complete paralysis of the bladder, which necessitates catheterization. Bilateral section of the spinothalamic tracts (Grant, 1931), which does not necessarily cripple the bladder, is equally effective and is also an easier and a less dangerous procedure. For the distinctly poor risk patient with carcinoma of the bladder and prostate which has not spread into the neighboring tissues (*i.e.*, where the pain is limited to the external genitalia, perineum, and perianal region) White (1938) has advocated a modification of intrathecal alcohol injection. This is carried out with the patient lying in the prone position and the table adjusted so that the lumbosacral spine is flexed and the caudal end of the subarachnoid space uppermost. One to 1.2 cc. of absolute alcohol injected in this position through a low lumbar interspace causes a consistent paralysis of the three to four lowest sacral nerves with relief of pain referred to these dermatomes. The anal sphincter becomes patulous, but no weakness of the legs has resulted and impairment of bladder function has not necessarily followed. When patients already have suprapubic drainage or an inlying catheter, this procedure is far superior to resection of the inferior hypogastric ganglia and it is of outstanding value in certain sufferers who are too sick to tolerate a cordotomy.

Operations for Intractable Ureteral and Kidney Pain. Early studies on ureteral sensation were made by Head (1893), who mapped out areas of referred pain over the two highest lumbar spinal segments. Wharton (1932) has studied the nerve supply of the ureters in the human fetus by a special clearing and staining technic. His dissections show that they receive a nerve sup-

bined with dissection and lateral transplantation of the ureter is indicated. Many kidneys which have finally been resected might have been saved in this way.

Relief of Dysmenorrhea and the Pain of Uterine Malignancy. The nerve supply of the uterus differs from that of the bladder, because the greater portion of its visceral afferent nerves run through the superior hypogastric plexus. The nerve fibers in the walls of the uterus are derived from the plexuses of Frankenhaeuser, which are situated in each broad ligament. These are made up of filaments from both the superior and inferior hypogastric plexuses. The ovaries derive their chief nerve supply from the fibers which leave the intermesenteric and renal plexuses and follow the ovarian arteries. In the suspensory ligament the ovarian plexus divides into a number of external branches which surround the Fallopian tube, and other internal fibers which enter the ovary. The nerves that supply the vagina arise from the anterior part of the hypogastric plexus and from a few sacral root filaments. This brief anatomical description is based on an excellent English review of the work of the French neuroanatomists which has been published by Fontaine and Herrmann (1932) and on the monograph by Reynolds (1939).

It has been the classical teaching that the superior hypogastric plexus exerts a vasoconstrictor effect on the pelvic viscera, while vasodilatation is mediated by the sacral autonomic fibers. However, the exact nervous control of the uterine musculature is still unknown. Resection of the superior hypogastric plexus does not alter the normal menstrual cycle, but according to Fontaine and Herrmann may precipitate a single atypical period within the first few days after operation. This is probably induced by the intense uterine hyperemia which follows pelvic sympathectomy, and should not be regarded as true menstruation. Subsequent periods appear at the usual date after the last preoperative flow. Numerous postoperative observations have shown that pregnancy and parturition are not affected by presacral neurectomy.

The fact that section of the sympathetic genital nerves causes no detectable change in uterine physiology points to the conclusion that they carry mainly visceral sensation. The experimental studies of Leriche and Stricker (1927) give clear-cut evidence of this in animals. Cleland (1933) has shown, both in

pedicles (Fig. 18). Denervation of the kidney causes no obvious change in urinary secretion (see p. 95), but is effective in interrupting pain of renal origin. Hess (1930), Stone (1934), Peirson, and Deming (see discussion of Stone's paper) have reported lasting relief of renal pain by decapsulation and stripping the nerves from the renal vessels. The nerves should be dissected off the greatest possible length of the vessels, in order not to miss some of the delicate fibers and to prevent regeneration. In view of what is known concerning the capacity of the visceral nerves to regenerate, this is of major importance. In a communication from Peirson he has stated that one of his patients had a recurrence of pain a number of months after operation, most likely the result of nerve regeneration.

We have only a single case to illustrate this procedure:

Mrs. Helen C, 39, B.M. #6814. This patient was referred by Dr. E. L. Peirson, Jr. of Salem and was treated in collaboration with Dr S. B. Kelley of the urological service. The patient complained of dull aching pain in the left kidney region which radiated forward over her lower abdomen. At times this pain became sharp and stabbing, so that she was forced to take to her bed for several days. A year prior to admission to this hospital Dr. Peirson had removed a pair of infected Fallopian tubes, but her pain had not been relieved. On cystoscopy Dr. Peirson had found it possible to reproduce her pain by overdistention of the left renal pelvis, and x-rays taken with opaque media showed spasm of the upper ureter. On admission to this hospital deep palpation in the left upper quadrant produced local tenderness.

Paravertebral procaine block of the lowest thoracic and upper lumbar sympathetic ganglia relieved the patient's symptoms for one hour. It was therefore decided to explore the left kidney with the assistance of Dr. Kelley and to denervate the renal pedicle and upper ureter if no local pathology could be found

These procedures were carried out on 1/5/38. The kidney had a long pedicle so that it was possible to do a thorough exploration. This revealed no gross pathology The renal artery, veins, and upper 3 cm. of ureter were then carefully dissected free of all surrounding nerves, which were resected over a wide area. On discharge a fortnight later the patient was free of her old pain and has remained so during the following twenty-two months.

From a review of published cases and this instructive experience it seems logical to recommend exploration for obscure pain in the kidney. In the event that no obvious pathological condition is found, perivascular neurectomy of the pedicle com-

should be taken to carry the dissection down to the origin of the internal iliac arteries, in order not to miss the rami from the fourth lumbar ganglia which run under the iliac artery and vein on each side (Fig. 19).

A most instructive report on the value of presacral neurectomy in essential dysmenorrhea has been published by Meigs (1939) from this hospital. He is the only surgeon who has given statistics on a series of patients in whom the superior hypogastric plexus has been resected without any other pelvic surgery to becloud the issue. Of his 20 patients, 15 had a successful result.* There were partial successes in 2 other cases and 3 were complete failures. However, in the ordinary patient who fails to respond to non-operative gynecological measures, Meigs recommends that in addition to the neurectomy the surgeon should routinely dilate the cervix, suspend a retroverted uterus, and correct any other pathological process he may find in the tubes and ovaries. He concludes that this operation is the best form of treatment for patients with true primary dysmenorrhea.

In spite of the fact that a number of papers have advocated resection of the superior hypogastric plexus for pain in malignant disease of the fundus and cervix (Fontaine and Herrmann, 1932; Wetherell, 1933; Greenhill and Schmitz, 1933; and Adson and Masson, 1934), we cannot subscribe to this view. In our experience cancer of the uterine cervix and fundus is not painful until the disease has spread out into the paracervical and parametrial tissues. In the first case the pain is transmitted over the lower sacral nerves. On the other hand, when the disease has spread laterally pain may also be referred over the ovarian pedicles from the broad ligaments or over the lumbosacral plexus when the carcinomatous cells have infiltrated the posterior wall of the pelvis. In either of these eventualities, cordotomy is the only logical operation.

* In one of these cases there has been a recent recurrence of painful menstruation after a four year period of relief.

dogs and in human beings, that uterine pain enters the spinal cord over the eleventh and twelfth thoracic roots. That this applies only to pain from the uterine fundus has been shown by Meigs (1939), who has tested uterine sensation after presacral neurectomy. Taking biopsies from the uterine fundus is then no longer painful, but sacral pain is still present when the cervix is dilated and tubal insufflation still causes discomfort in the right and left lower quadrants of the abdomen. The conclusions to be drawn from these observations are that cervical sensation is transmitted over the sacral nerves, as is pain from the prostate and bladder, whereas sensation from the Fallopian tubes is probably referred over the ovarian pedicles.

The etiological factor in the production of pain during the menses is not known. This subject is discussed by Davis (1938) in his monograph on dysmenorrhea. He believes the cause of the pain to be the muscular contractions of the uterus, which may be of either hormonal (pituitary and ovarian) or neurogenic origin, and that "the pain may be due to exaggeration of either motor or sensory impulses by a nerve rendered hypersensitive through inflammation."

In the search for a practical operation for the relief of painful menstruation and carcinoma of the uterus, Jaboulay (1899) first attempted to interrupt the nerves through a perineal incision. Leriche (1925) developed a more successful method by performing periarterial sympathectomy on the internal iliac arteries. This operation gave complete and lasting relief from pain in most cases of dysmenorrhea, but has been simplified by Cotte (1925), who advocated the present method of resecting the superior hypogastric plexus. Very gratifying results have been reported after this operation in intractable dysmenorrhea. Fontaine and Herrmann (1932) have reported 22 operations for dysmenorrhea with only 2 failures from Professor Leriche's clinic in Strasbourg. According to Davis (1938), 75 per cent of the patients with uncomplicated dysmenorrhea are cured by presacral neurectomy and the majority of the others are greatly relieved. This statement is in agreement with a large number of other reports in recent medical journals. The patients must be carefully selected to exclude pain from the ovaries and other related structures, and the resection of the hypogastric plexus must be complete. In performing the operation particular care

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PART III

INTRODUCTION

In order to produce lasting physiological results, sympathetic denervation of an extremity or viscus must be anatomically complete and carried out in such a way that regeneration cannot take place. Following an incomplete denervation, the remaining intact autonomic fibers are capable of liberating a chemical mediator substance at their endings which stimulates the denervated smooth muscle cells and thereby may bring about a recurrence of the original disorder (see p. 118). In order to prevent regeneration, a considerable length of sympathetic trunk or splanchnic fibers must be removed. The powers of regeneration are particularly remarkable in the preganglionic fibers. Gibson (1940), who has made a microscopic study of the sympathetic synapse, has observed degeneration of the boutons (fiber terminations on the nerve cells) in the superior cervical sympathetic ganglion after proximal section of the trunk and their reappearance with the return of function forty-four days later. In experimental animals division of the cervical sympathetic trunk and transplantation of its two ends to opposite sides of the sternomastoid muscle is followed by regeneration within a month. Lee (1930) has described regenerating axons finding their way through the substance of the muscle. Tower and Richter (1931 and 1932) have shown that cutaneous galvanic reflexes, characteristically abolished when the sympathetic axons are paralyzed, return within a month after cutting the preganglionic rami to the stellate ganglion. But after interrupting postganglionic fibers they observed no return of central activity within a period of eighteen months. These findings are almost identical with those recently reported by Hinsey, Phillips, and Hare (1940). But Haimovici and Hodes (1940) have presented evidence for regeneration even after removal of the entire sympathetic chain on both sides. Simmons and Sheehan (1939) and also Smithwick (1940) have reported many instances of recurrent sweating and vasomotor

activity after cervicothoracic ganglionectomy with removal of the inferior cervical, first, and second thoracic ganglia. How preganglionic axons can bridge the gap left by the removal of the cell bodies of the postganglionic neurons is difficult to understand and no histological explanation has yet been given, but if delicate tests are used to demonstrate recovery, such as rise in surface temperature on diagnostic procaine block and fluctuations in electrical skin resistance, a greater or lesser degree of regeneration can be demonstrated in a surprising proportion of patients.* According to Sheehan (1941) it is conceivable, though unlikely, that preganglionic fibers could extend down into the arm and take over the functions of the postganglionic neurons. Foerster (1935) has suggested that the middle cervical ganglion may be a source of postganglionic neurons to the upper extremity, and such fibers would remain intact after the ordinary cervicothoracic operation. Another explanation has been offered by Livingston (1939), that in man a considerable number of postganglionic cells related to the arm lie in ganglia below the second thoracic; the operation would then merely interrupt their axons and regeneration could be readily effected. The problem of how to produce a lasting preganglionic denervation of the upper extremity has indeed been a difficult one. We hope that the method described on page 406 will effectively prevent regeneration. The resection of the second and third lumbar ganglia and intervening trunk is usually sufficient to insure a lasting sympathetic paralysis of the lower extremity, but regeneration is likely to follow a lesser removal. Ramisectomy alone cannot be counted upon, because regeneration is almost certain to take place.

The return of reflex control of blood pressure after extensive sympathectomy has recently been studied by Grimson, Wilson, and Phemister (1937). After complete sympathectomy in dogs these investigators observed a recovery in central control beginning within a few weeks and reaching the preoperative level in an average time of six months. They were unable to explain the nature of this vasoconstrictor mechanism, but concluded that, although gross evidence for regeneration of the nerves to

* These determinations have been made by Drs J E. Finesinger, A. P. Heusner, and G. Saslow with the technical assistance of Miss F. F. McGuire in the Psychiatric Laboratories of the Massachusetts General Hospital.

the trunk and extremities is meager, yet the possibility of preganglionic regeneration to outlying visceral sympathetic ganglia and the adrenals cannot be excluded.

The physiological importance of performing sympathetic denervation by interrupting the upper or premotor neuron in order to prevent the exaggerated compensatory response to adrenine and sympathin has been discussed in Chapter V.

The effective degree of vasodilatation which follows complete sympathetic denervation is most clearly brought out by quantitative measurements. Horton and Craig (1930) and Reichert (1933) have demonstrated the increased arterial caliber by arteriograms. Brown and Adson (1929) state that whereas the normal ratio of arterial wall to lumen is 1 to 2, after ganglionectomy it becomes 1 to 3.5. Heat elimination, measured by Brown (1926) in the extremities with the Stewart-Kegerreis calorimeter, is increased approximately 70 per cent. Herrick, Essex, and Baldes (1932) have determined blood flow in the legs of dogs by means of the Rein thermostromuhr; this very accurate method shows an average increase of 100 per cent in the denervated extremity tested from nineteen to thirty-four months after operation. Wagener (1931), by means of a special ophthalmoscope, has measured the dilatation of the retinal vessels after cervicothoracic ganglionectomy. In 36 cases of normal vessels he noted vasodilatation in all but one instance (a case of Buerger's disease), and found it still present at the end of a year. In our own cases we have observed elevation in surface temperature amounting to as much as 15 degrees five years after lumbar ganglionectomy. This has also been true of the patients after the newer preganglionic denervation of the upper extremity. Some of these patients have now maintained a complete vasodilatation for over four years.

The lasting results of complete visceral denervation in cases of pain have been all that could be wished. In patients with angina pectoris, in whom we have destroyed the upper four thoracic ganglia, or their cardiac rami, pain has disappeared (White, 1940). In 14 patients freedom from attacks has lasted for over two years, in 3 for over five years, and in 2 for as long as eight years.

With the awakened interest of clinicians and surgeons in the autonomic nervous system, this branch of neurosurgery is be-

ginning to emerge from its early phase of trial and error. Fifteen years ago knowledge of the anatomy and physiology of the human autonomic nervous system was uncertain, clinical reports uncritical, and prolonged follow-up statistics meager. Modern diagnostic tests, accumulation of more reliable case reports, and a better knowledge of the type of operation required to produce a desired physiological effect are the factors responsible for this development. The first two have been taken up in Parts I and II; the discussion of operative technic remains for this final section.

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Chapter XVI

CERVICAL SYMPATHECTOMIES

Resection of Superior Cervical Sympathetic Ganglion. In order to obtain a good exposure for this operation the patient should be placed on the operating table with his head rotated toward the opposite shoulder and the neck extended backward over a narrow pillow or bar (Fig. 66). Regional anesthesia is most satisfactory. It is induced by a subfascial injection of 1 per cent procaine along the posterior border of the sternomastoid muscle. This infiltrates the superficial branches of the cervical nerves and is usually sufficient, although at times it must be supplemented by a further injection around the carotid sheath. A 7 cm. oblique incision is made along the posterior edge of the sternomastoid muscle, starting at the tip of the mastoid process. The incision is carried through the platysma and superficial cervical fascia. The sternomastoid muscle is then retracted anteriorly and mesially and the carotid sheath freed. This exposes the vagus nerve, which runs in the vascular sheath behind the carotid artery and jugular vein. After these structures have been retracted forward, the cervical sympathetic trunk can be found lying just posteriorly on the longus capitis and longus colli muscles. While it usually adheres to the fascia on the muscle, it may occasionally be retracted forward with the carotid sheath.

Once the sympathetic trunk has been found, it should be elevated from its bed and the dissection carried upward. The *superior cervical ganglion is a fusiform structure about 3 cm. in* length, the upper pole of which runs almost to the base of the skull. It must be dissected out by careful blunt dissection, the superior cardiac nerve being cut, as well as the numerous gray rami which connect it with the upper three cervical nerves, the carotid plexus, and the closely associated glossopharyngeal,

spinal accessory, hypoglossal, and vagus nerves. As these connections are successively cut, the entire length of the ganglion can be drawn into view until it is possible to cut the rami at its upper pole without risk to other important structures which lie in the immediate vicinity. Hesse (1930) has advocated leaving intact the superior pole of the ganglion, the portion above

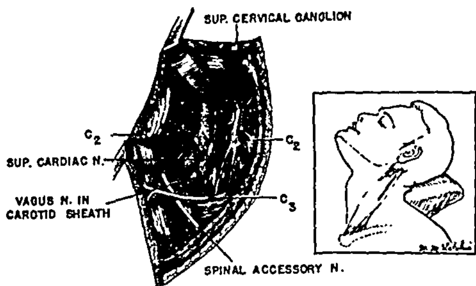


FIG. 66. Superior cervical ganglionectomy.

the superior cardiac nerve. With this modification the few remaining nerve cells are cut off from the central nervous system, and the rare but troublesome cervical neuralgia which may occur after total resection may be avoided.

We have seldom utilized this operation, because it gives only a partial interruption of the sympathetic pathways to the head and a very incomplete denervation of the heart. It has been advocated for: (1) Facial paralysis, to produce a drooping of the upper eyelid and thereby enable the patient to close his eye. This is a really valuable procedure. (2) Angina pectoris: Resection of the superior cervical ganglion interrupts but few motor and probably no direct sensory fibers to the spinal cord, and its resection is of questionable value, even when pain is referred to the head and neck (see Chap. XI).

Stellate Ganglionectomy. Jonnesco (1923), Brüning (1923), Royle (1932), Gask (1933), and Leriche and Fontaine (1933) have been the leading advocates of the cervical approach for

stellate ganglionectomy. Resection of the stellate by this route is carried out with the patient in the same position as for resection of the superior cervical ganglion. Intratracheal ether-oxygen insufflation is the safest anesthetic, as by this means the risks of pneumothorax in case the pleura is opened are eliminated.

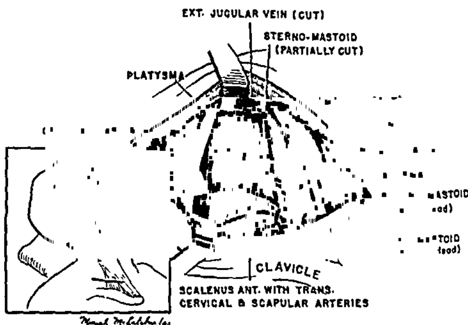


Fig. 67. Cervicothoracic ganglionectomy by the cervical approach. 1. Exposure of the vascular structures and the anterior scalene muscle.

The most satisfactory exposure is that described by Royle (1932) and further developed by Gask (1933). A transverse incision is made a finger's breadth above the clavicle and carried laterally 5 cm. from the sternal tendinous head of the sternocleidomastoid muscle (Fig. 67). The thin clavicular head of the muscle is divided (and later resutured). This centers the incision over the vertebral artery. The omohyoid muscle, which runs obliquely across the field, is cut across and the deep cervical fascia opened. The carotid sheath lies on the medial side of the incision, while the floor is formed by the anterior scalene muscle (Fig. 68). After retracting the carotid sheath and phrenic nerve toward the midline, the muscle is cut across just above its insertion in the first rib. This is the key to obtaining a sufficiently deep exposure to insure the resection of the upper three thoracic ganglia. In addition it gives a clear view of the proximal por-

tion of the subclavian artery, the origin of its thyroid axis and vertebral branches, as well as the lower end of the common carotid (a branch of the subclavian on the right and a separate trunk on the left). After ligating and cutting the thyroid axis, the central end of the subclavian artery is next thoroughly freed up by blunt dissection in order to obtain a clear view of the tissues behind the origin of the vertebral artery. The stellate ganglion lies just at this point adherent to the lateral surface of the seventh cervical and first thoracic vertebrae (Fig. 9).

In a left-sided incision the thoracic duct should be identified and retracted out of the field with a thin ribbon retractor. The duct runs forward out of the depths of the mediastinum from behind the jugular vein and enters the subclavian just lateral to its junction with the jugular. This stage of the operation requires an absolutely bloodless field and the best available illumination from either a lighted retractor or headlight. Needless to state, considerable care must be taken not to puncture the apex of the pleura nor injure the thoracic duct or one of the large blood vessels. In order to expose the sympathetic chain as low as its third thoracic ganglion, which is about the maximum extent of trunk which can be resected by this approach, the surgeon should next cut Sibson's fascia, which attaches the apex of the pleura to the posterior portion of the first rib. When this step has been carried out, the entire apical pleura can be readily freed by blunt dissection to a point as low as the third rib. It is then a simple matter to visualize the inferior cervical and first thoracic ganglia (Fig. 68). This double ganglion is usually a dumbbell-shaped structure, 1.5 to 2.5 cm. in length, and made up of the two ganglia connected by a distinct isthmus, although at times both portions are fused into a single mass. Its lower portion lies immediately in front of the first thoracic nerve and against the head of the first rib. Its upper pole ends in a number of fine rami which connect it with the lower trunks of the brachial plexus. These star-shaped rami have given it the name of stellate ganglion and make its identification an easy matter. When this structure has been freed from its bed the chain can be followed down as far as the third thoracic ganglion with very little difficulty.* Once this upper portion of the sympathetic chain has

* Care should be taken at this point not to injure the highest intercostal artery, which is a large branch of the costocervical trunk of the subclavian.

been exposed, the best method of dealing with it depends on the purpose to be accomplished. In angina pectoris and certain neuralgias of the upper extremity the entire length of trunk should be resected. In Raynaud's disease it is important to preserve these ganglia, which contain the cell stations of the postganglionic fibers to the lower cords of the brachial plexus, in order to prevent excessive sensitization to sympathomimetic

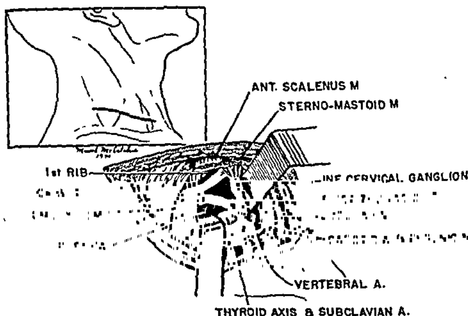


FIG. 68 Cervicothoracic ganglionectomy by the cervical approach.

2. The scalenus anticus muscle has been divided and the subclavian vessels and dome of the pleura retracted downwards. The retraction of these structures has been purposely exaggerated in order to show the first thoracic ganglion.

hormones (see Chap. V). A method by which this can be done and the central preganglionic vasoconstrictor fibers interrupted has been described by Telford (1935). In this operation the chain is cut at the level of its third thoracic ganglion. The gray and white rami which connect the second and third ganglia with the intercostal nerves are also divided. In this way all spinal vasoconstrictor and sudomotor fibers to the arm and head are cut, but the oculopupillary fibers are preserved. In order to minimize the likelihood of regeneration, the cephalic end of the trunk is swung up and sutured into the cervical incision.

After the completion of either of these procedures and after all bleeding points have been dealt with, the incision is closed in

layers without drainage. The clavicular head of the sternocleidomastoid muscle is resutured, but the separated ends of the scalenus anticus cannot be approximated.

Telford's (1935) modification of preganglionic sympathectomy carried out through this approach has not proved to be a successful method of dealing with Raynaud's disease, because ultimate regeneration often takes place (see Chap. VIII). It is probable that the use of Smithwick's modification of enclosing the upper centrally disconnected portion of the trunk in a silk sleeve (see p. 406) will be effective in preventing regenerating preganglionic fibers from growing back into the decentralized cervicothoracic ganglia, but we have not had time to check this up. Because this operation does not permit excision of the second and third anterior spinal roots well back within the dura, we believe that this method can never as surely prevent regeneration as does Smithwick's modification of the posterior approach, which is described below.

Preganglionic denervation of the upper extremity by the cervical approach is a satisfactory method for dealing with hyperhidrosis, because recurrence of sweating has never been extensive. But we have preferred the posterior approach simply because of greater experience with it. The cervical operation is also a useful method for dealing with causalgia, painful traumatic arthritis, and amputation stump neuralgia, when these conditions are associated with vasospasm and respond to diagnostic procaine block. We also believe that the cervical approach for the inferior cervical and upper thoracic sympathetic ganglia is the safest operative method for effecting a complete sympathetic denervation of the heart in angina pectoris.*

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* Whether there are cardiac rami below the third thoracic ganglion is not yet known with certainty. It is our opinion that connections from the fourth and even the fifth thoracic ganglia are occasionally present, but that they are of minor importance.

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CHAPTER XVII

THORACIC SYMPATHECTOMIES

Upper Thoracic Sympathectomy. The relief of vasospasm in the upper extremity is a frequent indication for thoracic sympathectomy. Previous to 1935 we, as well as most others, preferred the operation of cervicothoracic ganglionectomy, in which the lowest cervical and upper two thoracic ganglia and intervening trunk were removed. The posterior approach was used. The results of this operation (postganglionic sympathectomy) were not satisfactory because vascular spasm still persisted to such a degree that neither we nor the majority of patients felt that the improvement was sufficient to justify the procedure. This matter of sensitization to adrenine and sympathin is discussed in detail in Chapters V and VIII. On the other hand, the results of lumbar ganglionectomy (preganglionic sympathectomy) were so uniformly satisfactory that it seemed desirable to devise a similar method for denervation of the upper extremity. This was reported by Smithwick (1936) and has been used continuously in this hospital since January, 1935. The immediate results are far superior and compare favorably with those following denervation of the lower extremity. There is, however, a much greater tendency for regeneration so that significant degrees of relapse have necessitated changes in technic to overcome this difficulty. This matter is reviewed in Chapter VIII, and is illustrated in Figures 52 and 53. It has been discussed in detail by Smithwick (1940*A* and *B*).

It is of interest that Telford (1935) independently came to similar conclusions regarding denervation of the upper extremity, and devised an almost identical operation using an anterior approach. Simmons and Sheehan (1937 and 1939) have studied the results in many of his cases, and found also that the immediate effect was most satisfactory, but that there was a marked tendency to regeneration. We have employed the

anterior approach at times, particularly when section of the scalenus anticus muscle or excision of an anomalous first or cervical rib was indicated. The technic is described in Chapter XVI.

In both operations the principle is the same and consists of the decentralization of the second and third dorsal ganglia by dividing the trunk below the latter and the rami communicantes to both, displacing the upper sectioned end of the trunk as far as possible from the lower. In Telford's operation the cephalic stump is brought up into the neck: in Smithwick's it is brought out of the thorax and sutured into the posterior wound. The first thoracic rami are not divided in either, consequently a Horner's sign is not produced. There is no evidence that the first thoracic white ramus carries either vasomotor or sudomotor fibers of consequence to the upper extremity in man. The ganglia are not removed in either operation, as this would cause degeneration of postganglionic fibers and maximal sensitization to sympathomimetic hormones. Only the preganglionic pathways to the arm are divided. The modification which we have made to prevent regeneration, in which the second and third ganglia are encased in a silk cylinder, can be used in connection with either operation (Figs. 71 and 72). We prefer the posterior approach because the second and third ganglia are much more accessible and this facilitates technical maneuvers designed to prevent regeneration.

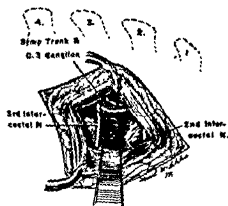


Fig 69 Preganglionic sympathectomy by posterior approach. Sympathetic trunk and intercostal nerves exposed.

Incision is centered opposite space between second and third thoracic spinous processes The inner portion of the third rib has been removed and the pleura separated, exposing the second and third intercostal nerves and the sympathetic trunk (From Smithwick, 1940C, courtesy of *The New England Journal of Medicine*)

Denervation of Arm by Preganglionic Section—Operative Technic. The technic for denervation of the upper extremity has recently been described in detail by Smithwick (1940C). The patient is placed in the prone position, the chest supported by

pillows in such a way that the shoulders slump forward, the abdomen free from pressure, and the neck flexed forward slightly so that there are no wrinkles in the skin. Under intratracheal anesthesia, a paravertebral incision is made, 7 cm. long and about 5 cm. lateral to the midline. It is centered opposite the space between the second and third thoracic spinous processes. The trapezius fibers are divided transversely for 3 cm. in the center of the wound. The underlying rhomboid muscle is split in the direction of its fibers. A finger can then be passed upward and downward beneath this muscle, and the third rib accurately identified. The inner 5 cm. of this rib is removed through a split in the longissimus cervicis muscle. The tip of the transverse process is resected and the underlying rib fragments beveled. The pleura then is gently separated to the midline of the vertebral column, to above the second rib and to a point below the fourth rib (Fig. 69).

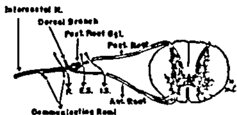
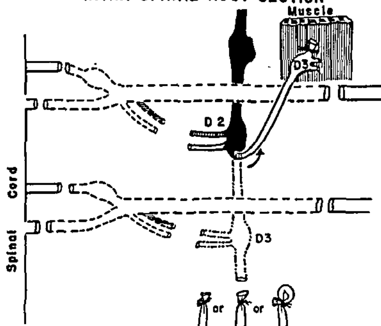


FIG. 70. Various methods of interrupted sympathetic outflow from the second and third thoracic segments.

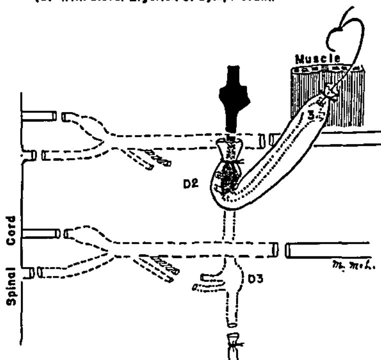
In technic R., the point of proximal section of the second and third intercostal nerves is lateral to the posterior root ganglion. In E.S., the anterior and posterior roots are divided separately at a point just medial to the posterior root ganglion. In I.S., the posterior root is sectioned as in E.S., but the anterior root is divided more medially within the arachnoid. In all instances the rami communicantes are divided and a 5 cm. segment of the second and third intercostal nerves is removed. (From Smithwick, 1940C, courtesy of *The New England Journal of Medicine*.)

The third intercostal nerve is next divided at the lateral border of the incision. Dissection is carried medially along the nerve, dividing first the gray ramus, second the dorsal branch, and finally the white ramus. The posterior root ganglion is then clearly seen at the mouth of the intervertebral foramen. A dental spatula can be slipped between the anterior and posterior roots. The latter is divided just proximal to its ganglion, exposing the anterior root as the sole remaining structure. The meninges are gently pushed medially along this root until the white, glistening intradural portion is brought into view. This is divided, the proximal end retracting within the arachnoid. A spinal fluid leak of no consequence results from this maneuver. A sketch of a typical specimen of an intercostal nerve removed is shown in Figure 70. This is called intraspinal root sec-

INTRA SPINAL ROOT SECTION



(a) With distal Ligation of Symp. Trunk



(b) Covering of Decentralized Ganglion D2 & D3 with silk cylinder

FIG 71. Diagrammatic representation of preganglionic sympathectomy—upper extremity

(From Smithwick, 1940*B*, courtesy of *Annals of Surgery*.)

tion (I. S.), because the anterior root is divided within the arachnoid. When the roots are sectioned just proximal to the dorsal root ganglion, the term extraspinal root section is used (E. S.). When the intercostal nerve is divided lateral to the posterior root ganglion, the term ramisectomy is used (R). The rami to the second and third ganglia are divided in all instances. Technic I. S. has been the most effective in preventing regeneration, but since adoption of the silk cylinder its use has been combined with all three methods of interrupting the outflow from T_2 and T_3. Technic R is the easiest and we hope may prove adequate when combined with the silk cylinder.

The same procedure is carried out in the case of the second intercostal nerve. The sympathetic trunk is then divided below the third ganglion and the distal end ligated within the thorax, either with a dural clip or silk, at times directing the cut end distally (Fig. 71). The decentralized second and third thoracic ganglia are covered with a fine silk cylinder to further guard against regeneration and the distal end of the cylinder is brought out of the thorax and sutured into the wound (Fig. 72).

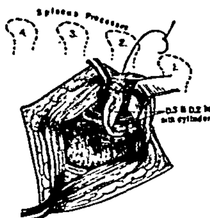


FIG. 72 Preganglionic sympathectomy by posterior approach. Final step.

The distal end of the silk cylinder, within which the decentralized second and third thoracic ganglia lie is brought out of the thorax and sutured into the wound. (From Smithwick, 1940C, courtesy of *The New England Journal of Medicine*.)

Occasionally an opening in the pleura is inadvertently made. It is best not to try to close it; no difficulty will be encountered if the lung is fully expanded and the extrapleural air space obliterated. This maneuver is facilitated by introducing a small soft rubber catheter through the opening in the pleura, and closing the wound about it. The intrapleural and extrapleural air is then gently aspirated through the catheter as the latter is withdrawn. Drainage is never instituted. Silk-suture technic is used. The upper extremities are always denervated separately, about a week apart. There have been no deaths. Between January 24, 1935, and January, 1941, 158 upper extremities (90 patients) were denervated by

this type of operation. The silk cylinder has been employed in the denervation of 20 extremities (15 patients) between February, 1940, and January, 1941. No untoward effects have followed its use.

Splanchnicectomy. This operation is most commonly used in *connection with the surgical treatment of essential hypertension.* It is occasionally used for the relief of abdominal pain and in congenital megacolon (Chap. XIV). Depending upon the technic employed, the motor and sensory innervation of the various abdominal viscera may be partially or completely interrupted. Since the general subject of hypertension has been presented in detail (Chap. XII), this discussion is concerned only with surgical technic.

Four operations are in common use at the present time. Peet (1935) resects the lower three thoracic ganglia and intervening trunk, thereby interrupting the lesser and least splanchnic nerves. In addition the great splanchnic nerve is resected as extensively as possible. These structures are exposed by removing the inner 5 cm. of the eleventh rib through a paravertebral incision placed about 5 cm. lateral to the midline. This is carried out on both sides, usually at the same time. The operation does not result in significant postural blood pressure changes. It is entirely confined to the supradiaphragmatic region, which does not afford opportunity for exploration of the kidneys or adrenal glands. The upper lumbar splanchnic connections cannot be removed, and the twelfth thoracic ganglion is reached with difficulty, if at all. On the basis of clinical results, it appears extensive enough to guard against regeneration. Peet, Woods, and Braden (1940) have reported in detail the effect of this operation in a series of 350 cases.

Craig (1934), and Allen and Adson (1940) have advocated a subdiaphragmatic approach through a slightly modified kidney incision, resecting the inner portion of the twelfth rib. The splanchnic nerves are resected as extensively as possible beneath the diaphragm, and the upper two lumbar ganglia are removed as well. The operation is performed bilaterally in two stages, a week or two apart. It has the advantage of permitting exploration of the kidneys and adrenal glands and removal of the upper lumbar splanchnic supply. It results in a significant postural fall in blood pressure in some of the cases. It does not,

in our hands, allow a sufficiently radical resection of the splanchnic nerves to guard against regeneration, and at times uncertainty exists as to whether all of the latter have been identified, particularly in obese or muscular individuals. Furthermore, it does not permit resection of thoracic fibers from the great splanchnic nerve which appear to descend upon the aorta to the celiac plexus, and which may at times be important (Fig. 58).

Crile (1938) advocates division of the great splanchnic nerve with resection of the celiac ganglion. This is performed through a flank incision curving slightly forward, starting below the tip of the twelfth rib. It is done in two stages, a week or two apart. The major and lesser splanchnic nerves and celiac ganglion are identified, the connections of the latter to the plexus divided, and finally the great splanchnic trunk cut with scissors and the ganglion removed. This operation has the advantage of permitting exploration of the kidneys and adrenal glands, but as it is carried out by tactile sense rather than by direct visual identification of the structures, there is no certainty that the lesser and least splanchnic nerves are divided, as they do not necessarily enter the celiac (semilunar) ganglion. The upper lumbar splanchnic supply is not interrupted. This does not completely denervate the splanchnic bed, and postural blood pressure changes do not follow. Regeneration may be delayed, but ganglionectomy does not necessarily prevent this. In addition the operation is largely a postganglionic type of denervation to which there are theoretical objections.

Personal experience with both supra- and infradiaphragmatic approaches, coupled with a careful study of the clinical results and further consideration of the anatomical distribution of the sympathetic pathways concerned (Chap. XII, Fig. 58), have led to the development of a new technic (Smithwick, 1940*D*) which appears to combine the advantages of both operations. It permits resection of the sympathetic trunk from T_9 to L_2, and of the great splanchnic nerve from its insertion in the semilunar ganglion upward to the midthoracic region. The kidney and its pedicle are very accessible, so that careful study of gross pathology can be made, renal venous blood taken for study, and biopsies of renal parenchyma taken in selected cases. The result of these studies may prove significant. The adrenal glands may be examined, and tumors may be removed with facility. This opera-

tion results in profound postural blood pressure changes, and appears to produce a very complete type of denervation. It is more extensive than the other operations, requires a little longer time to perform, but does not appear to carry a higher mortality. The latter is surprisingly low for all technics. Rare fatalities are chiefly due to cerebral accidents or cardiac failure. The combined mortality of all cases in the literature has been reported to fall between 2 and 3 per cent.

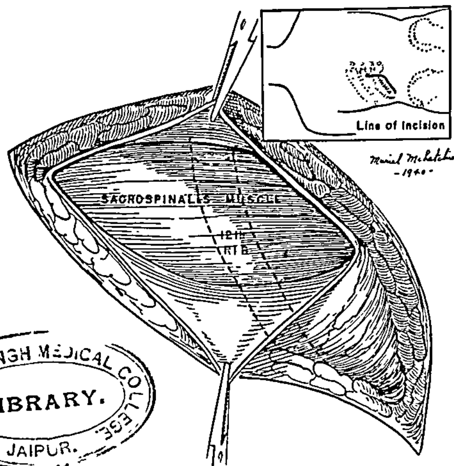


Fig. 73 Thoracolumbar splanchnicectomy
1. Line of incision.

Technic for Thoracolumbar Splanchnicectomy. The technic of this combined supra- and infradiaphragmatic splanchnicectomy is as follows: The patient is placed in the prone position, the chest and pelvis being supported so that there is no pressure upon the abdomen. The table is broken to flatten the lumbar

spine. Intratracheal anesthesia should always be used. A hockey stick incision is made. The upper portion is vertical, about 5 cm. from the midline, and runs downward from above the eleventh rib over the lateral portion of the sacrospinalis muscle group to below the twelfth rib; it then curves laterally about 1.5 cm. below the rib and extends approximately to the posterior axillary line, 7 to 10 cm. beyond the lateral border of the sacrospinalis muscle (Fig. 73). The sheath of the sacrospinalis muscle is

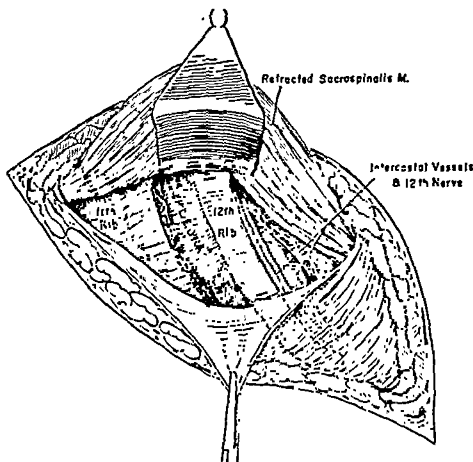


Fig. 74. Thoracolumbar *splanchnicectomy.*
2. Exposure of twelfth rib, intercostal vessels and nerve.

opened vertically to below the twelfth rib, and the incision then curved laterally through the deeper structures to a point beyond the tip of the rib. The sacrospinalis muscle is retracted medially, exposing the central end of the underlying rib (Fig 74). The rib is resected from the transverse process to the lateral

border of the sacrospinalis sheath. The twelfth intercostal artery, vein, and nerve are removed over a similar extent. The renal fascia is then incised just lateral to the diaphragm and the latter divided medially to the crus, together with the renal fascia which is adherent to its under surface. This incision should be made 2.5 cm. below and parallel to the pleural reflec-

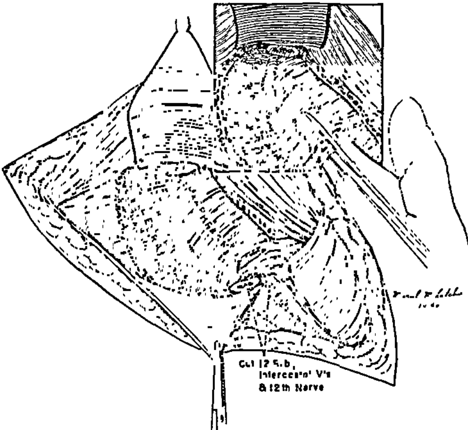


Fig 75. Thoracolumbar splanchnicectomy
3 Division of diaphragm.

tion (Fig. 75). It is important not to separate the renal fascia from the diaphragm as leaving this layer intact greatly facilitates resuture. The kidney (Fig. 76) with its pedicle, pelvis, and ureter, the adrenal gland, and the sympathetic supply are thus all readily visualized, and the desired extent of the latter can be removed (Fig. 77). Tilting the table 20 to 30 degrees laterally away from the surgeon helps to bring the anterolateral aspect of the vertebral bodies and the nerves into better view. The

sympathetic trunk is removed from T_8 to L_1 inclusive. In the more advanced cases, L_2 is also excised on one or both sides. The pleura is separated from the central ends of the ribs to the midthoracic level largely by gentle manual dissection. It is also freed medially to the aorta or vena cava and laterally for several centimeters as well. This permits resection of the great splanchnic nerve from the semilunar ganglion upward to approximately the midthoracic level, and insures division of

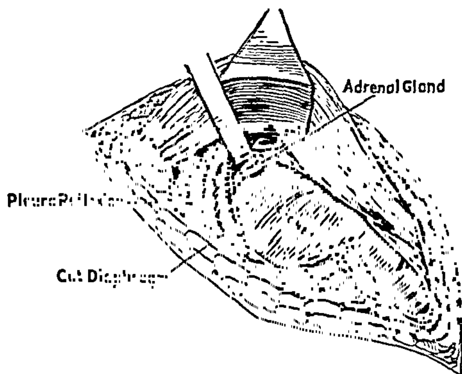


Fig. 76. Thoracolumbar splanchnicectomy
4. Exposure of kidney and adrenal gland

a variable number of branches of the great splanchnic nerve which are distributed to the aorta for some 15 cm. above the diaphragm. If the pleural cavity is entered, the lung is held gently inflated by positive pressure within the trachea. When the incision is closed any residual air within the pleural cavity or in the extrapleural space is aspirated by means of a soft rubber catheter and syringe, as described in connection with preganglionic denervation of the upper extremity. The diaphragm is then resutured with interrupted silk to approximately its original position (Fig. 78). The table is flattened to produce

a lumbar lordosis, which relaxes the muscles of the back and flank and permits closure of the rest of the wound in layers, without tension. Silk technic is used throughout. The operation is performed bilaterally in two stages, a week or two apart.

The postoperative convalescence is usually uneventful. A variable amount of hyperesthesia in the lower abdomen, flank,

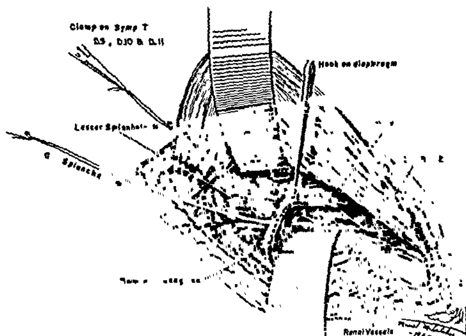


Fig :' .horacolumbar splanchnicectomy.
5. Exposure of sympathetic trunk and splanchnic nerves.

and lateral thigh usually appears five days to a week afterward, and may be quite troublesome for a few days. This can be minimized by using only the most gentle retraction in the region of the upper lumbar nerves. It is due in part to resection of the twelfth nerve, but the neuritis is even more marked if this nerve is left in place. After the second stage, increased peristalsis may be troublesome and can be combated by adequate doses of atropine. The patients are usually permitted to get up about two weeks after the second stage. Because of the profound postural drop in blood pressure, it is essential that both legs be bandaged from instep to knee, and that patients wear a snug lower abdominal binder with an underlying sponge rubber pad. These can gradually be eliminated, the leg bandages in

a few weeks, the sponge rubber pad in a month or two, and the abdominal girdle, as a rule, in about three months. We find the results of total and subtotal splanchnic denervation to be superior to partial splanchnicectomy for essential hypertension

Fig. 78 Thoracolumbar splanchnicectomy.
6. Suture of diaphragm and renal fascia.

(Chap. XII). No untoward effect has resulted from marked orthostatic hypotension. The abrupt change is greatly lessened in a period of weeks to months, but even as long as two years after operation blood pressure *may* fall to *low levels* when a patient stands without moving for as long as five minutes. Walking slowly will prevent this. The chief drawback is the delay in economic rehabilitation. In our experience the improved clinical results greatly outweigh this objection.

Other Indications for Thoracic Sympathectomy. The operation of cervicothoracic ganglionectomy is still used by some as a method of denervating the upper extremity for vascular

disease and allied disorders. The approach is similar to that for preganglionic section. As the purpose is to remove the inferior cervical and upper two thoracic ganglia, it is best to resect the second rib. The posterior approach is generally preferred in this country, while the anterior approach is regarded with favor in Europe. Excellent descriptions of surgical technic have been written by Adson and Brown (1929); Adson (1931 and 1934); and White, Smithwick, Allen, and Mixter (1933).

Removal of the upper thoracic ganglia or section of their rami in order to denervate the heart may be readily performed by resecting the second and third or fourth ribs. We resort to surgical excision for angina pectoris only in the rare cases when alcohol injection has failed or when the patient is an unusually favorable surgical risk. Under these circumstances we advocate the removal of the inferior cervical and upper three thoracic sympathetic ganglia and prefer to use the anterior cervical approach (see p. 399). This does not necessitate operating in the prone position, which we believe to be more hazardous in patients with angina pectoris, especially if they are obese and suffer from hypertension. This subject and other aspects of the treatment of angina pectoris are reviewed in detail in Chapter XI.

Occasionally, resection of the lower thoracic ganglia and splanchnic nerves is indicated for the relief of abdominal pain (see Chap. XIV). This can be best performed by a twelfth rib exposure as in splanchnicectomy for relief of hypertension. A thoracic approach to the communicating rami was devised by von Gaza (1924), and a subdiaphragmatic exposure was described by Craig (1934). Ramisectomy has been found effective in the relief of upper abdominal pain by both Archibald (1928) and Scrimger (1929), but it has no advantage over excision of the splanchnic nerves and sympathetic trunk from which they arise. Familiarity with the latter because of its use in the treatment of hypertension makes it the procedure of choice for the relief of abdominal pain of obscure origin.

Vagectomy. Intrathoracic resection of the pulmonary rami of the vagus nerves for bronchial asthma has been discussed on page 351. The operative technic was described in the first edition of this book (pp. 338–340), but since it is not a standard surgical procedure it has not been included in this edition.

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CHAPTER XVIII

ABDOMINAL SYMPATHECTOMIES

THE lumbar portion of the sympathetic trunk may be approached by either the transperitoneal or the retroperitoneal route. The principal indication for lumbar ganglionectomy is relief of vasospasm of the vessels of the lower extremity. The operation has a wide field of application, and its use dates to the observation of Royle (1924), who noted improved circulation in the leg in patients following lumbar ramisectomy for spastic paralysis. Temporary interruption of vasomotor pathways to the leg for diagnostic and therapeutic purposes may be induced by paravertebral procaine block. Alcohol may also be injected for its more prolonged but not permanent effect (Chap. XX). Flothow (1940) has recently discussed the relative merits of alcohol injection versus surgical excision of sympathetic pathways.

Transperitoneal Route. Previous to 1935 we used the transperitoneal approach routinely. Excellent descriptions of the technic have been published by Davis and Kanavel (1926), and Adson and Brown (1925, 1929). The transperitoneal approach is carried out under a general or spinal anesthetic with the patient in the Trendelenburg position. A paramedian incision is made, and the coils of small intestine gently packed and retained in the upper portion of the abdominal cavity by means of gauze moistened in warm salt solution. The chain on the left is exposed by mobilizing the sigmoid after cutting across its lateral peritoneal attachment. The sigmoid, together with its vascular supply from the inferior mesenteric artery, is reflected toward the midline by freeing its loosely attached mesentery from the posterior abdominal muscles. This separation is easily effected by the fingers, as in mobilizing the sigmoid prior to its resection in carcinoma of the colon. It is important to identify the

ureter and to have an assistant hold the sigmoid and small intestine well out of the way with his hand over a gauze pack. The aorta and upper portion of the left common iliac artery should be clearly exposed. The floor of this incision is formed by the psoas muscle, and its medial wall by the bodies of the lumbar vertebrae and the aorta. The genitocrural nerve runs obliquely downward over the belly of the psoas muscle.

The chain of lumbar ganglia lies just beneath the edge of the aorta in the gutter between the psoas muscle and the vertebrae. It is usually surrounded by a mass of lymphatic trunks and nodes, which at times resemble the chain of sympathetic ganglia. In searching for the sympathetic trunk it is usually best to identify the fourth lumbar ganglion, which lies beneath the edge of the common iliac artery at its bifurcation from the aorta. Once this has been located the chain should be freed gently by blunt dissection (small cotton pledgets on the end of a hemostat serve well for this purpose). The chain is cut off just above the fourth lumbar ganglion and grasped in a hemostat. *It is then an easy matter to elevate the fibrous sympathetic trunk* and to free it from its bed and from the surrounding areolar tissue and lymphatics by careful blunt dissection. The sympathetic rami are divided with scissors as they appear. The trunk itself should be followed upward for a distance of from 6 to 8 cm. and cut off above its second lumbar ganglion.

The chain on the right can be exposed either by reflecting the cecum medially, or through an incision in the posterior peritoneum just lateral to the border of the vena cava. This more direct approach cannot be utilized on the left side because the inferior mesenteric artery is in the way. Whichever approach is used, it is most important to identify the ureter and to reflect it forward with the posterior peritoneum. The inferior vena cava is exposed and then retracted gently toward the midline. Care must be taken not to injure the lumbar veins, which leave the vena cava and run posteriorly either above or beneath the sympathetic trunk. The trunk itself bears the same relation to the vena cava and the common iliac vein that it bears to the aorta and common iliac artery on the left side. From this point on resection of the right lumbar ganglia and trunk differs in no way from the procedure on the left side. Resection on the right is slightly more difficult than on the left because of the

relative thinness of the vena cava and the presence of lumbar veins arching over the sympathetic chain.

The posterior peritoneal incisions on each side should be sutured with fine catgut as soon as the sympathetic chain has been resected and complete hemostasis assured. The operating table is then dropped back to a horizontal position, all gauze packs removed, and the intestines allowed to fall back into the pelvis. The abdominal incision is closed as in any routine laparotomy. It should be possible to complete the bilateral resection within one hour in all but exceptionally fat individuals.

Retroperitoneal Approach—General Considerations. Various incisions have been suggested for exposure of the lumbar sympathetic trunk by a retroperitoneal approach. Royle (1924), Leriche and Fontaine (1933), Flothow (1935), and Pearl (1937) have published slightly different procedures all of which are satisfactory. Atlas (1940) uses Pearl's approach but divides the trunk either above or below the third ganglion and displaces the distal end, burying it in the psoas muscle. The matter was discussed by Smithwick (1940*A* and *B*) who explained in detail the operative technic and the reasons why we have used this approach in preference to the transperitoneal since 1936. As a rule the lumbar trunk contains four ganglia, but anatomical variations are common. Study of the postoperative effects of interruption of various portions of the lumbar trunk has shown that removal of the first, second, and third lumbar ganglia results in complete sympathetic denervation of the thigh and leg. Removal of the second and third ganglia results in a nearly complete denervation of the leg from the knee distally, but the effect on the thigh is not necessarily complete. The former operation is preferable from the point of view of completeness, but may interfere with ejaculation in men, owing to excision of the first lumbar ganglion (see p. 96). Both procedures interrupt largely preganglionic fibers running to the leg below the knee, and both seem extensive enough to prevent regeneration of consequence. Removal of the fourth ganglion adds nothing to the completeness of the operation, and has the disadvantage of interrupting postganglionic fibers running to the lower leg. Most of these arise in the fourth lumbar and upper two or three sacral ganglia.

Sympathetic denervation of the lower extremity as described

above is adequate, is largely preganglionic in type, and insures against regeneration of interrupted nerve pathways. Excision of that portion of the lumbar trunk which includes its first, second, and third ganglia with division of the corresponding communicating rami is practiced as a routine procedure in women. In men, the first lumbar ganglion and its communicating rami are not disturbed unless it is thought that the underlying vascular problem justifies their removal. The clinical results, so far as relief of vascular spasm is concerned, are uniformly satisfactory. Between May 26, 1936, and January, 1941, 146 lower extremities (99 patients) were denervated by this technic. There was 1 death due to a pulmonary embolus.

It can be seen that the main purpose is to expose the upper portion of the lumbar sympathetic trunk. Experience has shown that this region is best approached by the extraperitoneal route. If both sides are to be done, the operations are spaced one week apart. This approach is far superior to the transperitoneal operation, which we used extensively up to five years ago. Such a laparotomy is a much more difficult task, and subjects the patient to unnecessary risk and discomfort. Its field of application must necessarily be narrowed to good-risk patients and to those who are certain to derive great benefit from it. Moreover, it is almost impossible to remove the first lumbar ganglion by this route, and often the second ganglion cannot be reached without difficulty, if at all. Frequently the third and fourth ganglia are removed, an undesirable step for reasons previously stated. The only advantage of the abdominal approach is that both lower extremities can be denervated at the same time. The many advantages of the extraperitoneal route far outweigh this.

Retroperitoneal Approach—Surgical Technic. Either general or spinal anesthesia is used. The latter gives excellent muscular relaxation, and perhaps has an advantage in heavily built individuals. Silk-suture technic is preferred. Drainage is never used.

The patient is placed on his side, with a kidney bar in place just above the level of the iliac crest. Both knees are drawn upward so that the thighs are approximately at a right angle with the abdomen. This relaxes the iliopsoas muscle group. A medium-sized pillow is placed beneath the undermost thigh, a second pillow is placed between the two thighs and the under-

most shoulder is drawn forward. All these steps tend to tilt the patient backward toward the operator. This position is maintained by a strap running diagonally over the legs just below the knees, and by a padded support placed against the sacrum and the back in the scapular region. The kidney bar is then elevated, widening the space between the twelfth rib and the iliac crest and stretching the external oblique muscle. This effect can be intensified by lowering the head and foot of the table slightly.

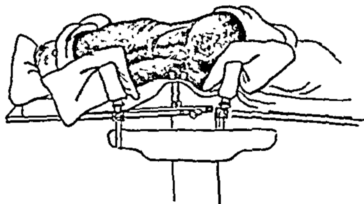


Fig. 79. Retroperitoneal lumbar sympathectomy.
1. Position of patient. Skin incision. (From Smithwick, 1940*A*, courtesy of *The New England Journal of Medicine*)

The final move is to tilt the table so that the plane of the patient's back is 30 to 45 degrees from the vertical position toward the surgeon. The latter stands facing the patient's back.

An incision is made starting in the angle formed by the twelfth rib and the sacrospinalis group of muscles (Fig. 79). It runs laterally 1 cm. below the rib to its tip, then curves downward over the posterior border of the external oblique muscle to the iliac crest. It meets the latter at a point about 3 cm. behind the anterosuperior iliac spine. In the posterior portion of the incision a variable number of fibers of the latissimus dorsi are cut across. The posterior border of the external oblique muscle is dissected out and retracted forward. This exposes the internal oblique muscle and its insertion into the lumbodorsal fascia. The fibers of the muscle and the fascia from which it arises are divided for a distance of 5 cm. This incision is made a finger's breadth below and parallel to the twelfth rib, and should open the lumbodorsal fascia from its origin from the quadratus lumborum and sacrospinalis group of muscles posteriorly to the

origin of the transversalis muscle anteriorly. The twelfth intercostal nerve lies just above and the first lumbar nerve just below the incision. The latter can be plainly seen running downward and forward along the lateral border of the quadratus lumborum muscle (Fig. 80). A finger is now inserted just below the twelfth rib, over the quadratus lumborum and psoas muscles, and posterior to the lower pole of the kidney and peritoneum. The finger meets the vertebral column in the region of the first lumbar vertebra. The sympathetic trunk is readily palpated on the anterolateral aspect of the spinal column. The finger is gently passed from above downward, separating the peritoneum from the psoas and quadratus lumborum muscles until the trunk has been exposed to a point below its third ganglion.

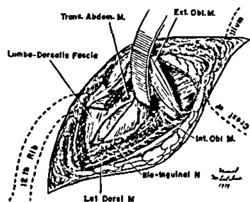


FIG. 80. Retroperitoneal lumbar sympathectomy.

2 Exposure and incision of lumbodorsal fascia. External oblique muscle retracted forward Underlying posterior fibers of internal oblique muscle incised for two centimeters Lumbodorsal fascia incised from origin of transversalis muscle anteriorly to underlying lateral border of quadratus lumborum muscle posteriorly (Modified from Smithwick, 1940*A*, courtesy of *The New England Journal of Medicine*.)

A long, moist strip of gauze is next inserted against the peritoneum, and the latter, together with the ureter, is then retracted upward and anteriorly with a long, curved retractor of the Dever type (Fig. 81). Because of the position of the patient one can look directly at the sympathetic trunk over the iliopsoas muscle group. It is not necessary to use posterior retraction except for lighting purposes. The sympathetic trunk is plainly visible, with its second and third ganglia and sets of communicating rami (Fig. 81). The first lumbar ganglion and its rami as a rule cannot be seen until the avascular fascia of the medial lumbocostal arch has been divided in an upward direction for about 2 cm. On the right side lumbar veins running into the vena cava may cross over the trunk. This is particularly true of a large constant branch just below the communicating ramus of the third lumbar ganglion. The desired portion of the sympathetic trunk and communicating rami can then be readily

removed. This step is facilitated by special instruments, long Crile hooks and Hartman forceps being particularly useful.

Retroperitoneal Approach to the Splanchnic Nerves. Craig (1934), Crile (1938), and Allen and Adson (1940) prefer this approach to the splanchnic bed. They have given their technic in detail and discussed the portion of the sympathetic nervous system which they consider most important in reference to the treatment of essential hypertension. This matter has been discussed in Chapter XII.

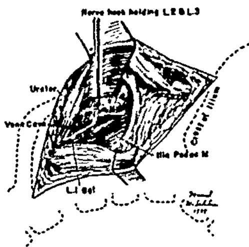


Fig. 81. Retroperitoneal lumbar sympathectomy.

2. Exposure of sympathetic trunk. The [illegible] two rami running from above downwards to the first ganglion. There are three rami connecting with the second ganglion. The latter is elongated and oval. The rami are short. The upper two run from above downwards from the second lumbar nerve to the ganglion. The lowest ramus runs from the ganglion in a caudal direction to the third lumbar nerve. Only one ramus connects the third ganglion with the fourth lumbar nerve. It is long and runs in a caudal direction. (From Smithwick, 1940A, *courtesy of The New England Journal of Medicine*.)

Resection of Superior Hypogastric Plexus (Presacral Neurectomy). The technic of resection of the superior hypogastric plexus has been standardized by Cotte (1925) and Learmonth (1931). A left paramedian incision is made from above the umbilicus to within 3 cm. of the os pubis. The patient is immediately tipped into pronounced Trendelenburg position, the incision spread open with a self-retaining retractor, and the coils of small bowel packed into the upper abdomen. This is greatly facilitated by the use of spinal anesthesia. The posterior peritoneum is incised vertically from a point 2 cm. above the bifurcation of the aorta to 5 cm. below (Fig. 82). Each lip of the peritoneal incision is then retracted. In this way the superior hemorrhoidal artery is drawn out of the way on the left side. In a thin subject the nerves can be readily seen lying in a delicate plexus of pelvic lymphatics and loose connective tissue. It is best to use blunt dissection and to clean out all the tissue in the hollow of the sacrum between the two common

iliac arteries. In carrying this out precautions must be taken not to injure the left common iliac vein, which lies on the medial side of the artery. Starting just beneath the aortic bifurcation, a strand of the presacral plexus is usually found as it descends over the left vein. It is picked up on a nerve hook, and as further strands are identified, first toward the median line and then nearing the right common iliac artery, they in turn are gathered on the hook.

The apex of the dissected triangle is now cut between the ligatures just above the bifurcation of the aorta. The peripheral

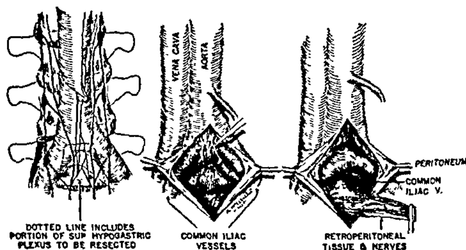


Fig. 82. Resection of the superior hypogastric plexus (presacral neurectomy). (Modified from Adson and Masson, *Journal of the American Medical Association*, 1934, CII, 986, with permission.)

end is then grasped and elevated by a hemostat and freed by blunt dissection with a cotton pledget. Communicating rami from the lower lumbar ganglia are severed in the process of wiping the plexus off the hollow of the sacrum. The dissection is carried downward until both common iliac arteries and the vein on the left side have been denuded over a length of 3 cm. The base of the triangle is then clamped and ligated. Ligation of the lower end of the pedicle is important in preventing seepage of lymph. The posterior peritoneum should be sutured with fine catgut, and the abdominal wall closed in layers in the usual manner. Careful examination of the triangular segment of tissue resected will reveal a variable number of nerve strands which constitute the superior hypogastric plexus.

It is important to remember in male patients that this opera-

tion is followed by loss of ejaculation. The power of erection and sensation of orgasm are in no way impaired, so that coitus can still be carried out, but the seminal fluid flows out very slowly. In the female there is no detectable change in sexual function.

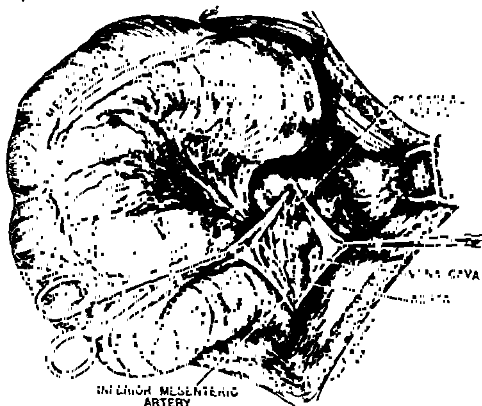


FIG. 83. Resection of inferior mesenteric and superior hypogastric plexuses for megacolon.
(Redrawn from Rankin and Learmonth, 1930, courtesy of *Annals of Surgery*.)

Resection of Inferior Mesenteric and Superior Hypogastric Plexuses. The operation of presacral neurectomy can be continued upward to include the resection of the small ganglia at the base of the inferior mesenteric artery and the periarterial sympathetic fibers which run along this artery to the descending colon and rectum. This procedure was first advocated by Rankin and Learmonth (1930) for denervation of the terminal large intestine in congenital megacolon.

In this operation the vertical incision through the posterior peritoneum is carried some 5 cm. upward along the aorta and above the inferior mesenteric artery (Fig. 83). In doing this

iliac arteries. In carrying this out precautions must be taken not to injure the left common iliac vein, which lies on the medial side of the artery. Starting just beneath the aortic bifurcation, a strand of the presacral plexus is usually found as it descends over the left vein. It is picked up on a nerve hook, and as further strands are identified, first toward the median line and then nearing the right common iliac artery, they in turn are gathered on the hook.

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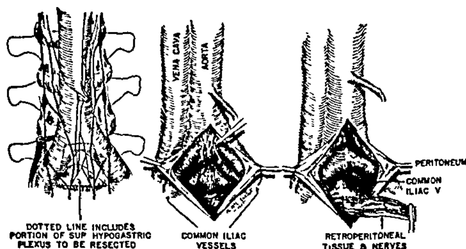


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It is important to remember in male patients that this opera-

malignant disease of the bladder and prostate, section of the spinothalamic pathways in the spinal cord is a more logical procedure. Cordotomy is more certain to give complete relief of pain in cases where tumor cells may be infiltrating the lumbosacral plexus, causes less damage to the emptying power of the bladder, and is a less formidable operation for the average neurosurgeon.

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care must be used not to injure the mesentery of the small intestine; in cases where it lies at an unusually low level it must be mobilized and retracted upward. The presacral plexus is freed by blunt dissection as described in the preceding section and cut off at its lower end. It is then a relatively simple procedure to follow the preaortic rami upward to the point where the right and left roots pass on each side of the inferior mesenteric artery. A pair of small ganglia is usually found at this point and should be resected. The proximal 2 cm. of the artery is then also denuded of the fine sympathetic fibers which surround it. The difficulty with this method of denervating the descending colon lies in interrupting all the fine nerve filaments which accompany the inferior mesenteric artery. The dissection must perforce be carried out by a blunt instrument in order to avoid injury to the blood vessels; in doing this it is extremely easy to miss some of the nerves, which may get pushed away from the artery and lost in the surrounding mesentery. For this reason we favor the bilateral resection of the lumbar sympathetic chains, combined with presacral neurectomy in female children.

More recently Leriche (1937) and Adson (1937) have advocated resection of the splanchnic nerves beneath the diaphragm in addition to bilateral lumbar sympathectomy on the grounds that the large bowel, the right colon in particular, derives a significant portion of its nerve supply from the splanchnic trunks.

Resection of Inferior Hypogastric Plexus. In order to carry out a complete denervation of the bladder it is necessary to cut the terminal rami of the hypogastric ganglia. In this way the sacral autonomic nerves, as well as the sympathetic plexuses, are destroyed. These ganglia lie in contact with the posterior wall of the bladder, the seminal vesicles, the ureters, and the anterior wall of the rectum. The ganglia are so adherent to the wall of the rectum that they cannot be safely excised.

Learmonth (1931) has described a method for subtotal denervation of the bladder by cutting the anterior branches of the ganglia. As this operation results in complete paralysis of the bladder and forces the patient to a catheter existence, it does not seem worth while to describe its technic. Although the operation is far more efficient than resection of the superior hypogastric plexus in interrupting pain pathways in cases of

CHAPTER XIX

PERIARTERIAL SYMPATHECTOMY AND DENERVATION OF CAROTID SINUS

Periarterial Sympathectomy. Jaboulay (1899) suggested dissecting the femoral artery from its bed in Scarpa's triangle and division of the vascular nerves which enter its sheath at this level. He stated that trophic ulcers in the feet could be healed by this procedure. His operation was modified by Leriche (1913), who advocated stripping the adventitial sheath of an artery with its perivascular plexus of nerves in order to produce vasodilatation. This type of periarterial sympathectomy has been applied by Leriche to all the larger arterial trunks, and consistently advocated by him and his associate Fontaine (1928, 1930, and 1933) for the treatment of a great variety of circulatory and painful disorders in the extremities. In spite of the enthusiastic reports which have emanated from Strasbourg and other French clinics, perivascular neurectomy has never been extensively adopted by British, German or American surgeons.* The reasons for this are based on fundamental anatomical and physiological concepts which deserve a thorough explanation.

Anatomical investigations of the vascular innervation conducted by Kramer and Todd (1914), Potts (1914), and more recently by Woollard and Phillips (1932), and Coates (1932) have taught us that the nerve supply to the arteries of the arms and legs, in contrast to that of the vessels in the thorax and abdomen, originates from the mixed peripheral nerves in a segmental manner. Figures 20 and 21 show that these vascular branches leave the main nerve trunks at short intervals and supply the perivascular plexus over a corresponding length of vessel. That this plexus does not run for any great distance

* Handley (1927), Doppler (1931), Herrmann (see Fontaine and Herrmann, 1933), Lehman (1934), and Homans (1940) are the outstanding exceptions.

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*Handley (1927), Doppler (1931), Herrmann (see Fontaine and Herrmann, 1933), Lehman (1934), and Homans (1940) are the outstanding exceptions.

down an artery has been shown on histological examination by Kerper (1927), and Busch (1929). In addition Blair, Duff, and Bingham (1930) made histological sections of the arteries of a human leg amputated after decortication of the femoral artery and found that the great majority of the fibers in the perivascular plexus of the lower leg were normal.

Physiological experiments have led to a similar conclusion. Rogers and Hemingway (1930) investigated the effect of periarterial sympathectomy by measuring heat elimination in a calorimeter and limb volume in a plethysmograph. Neither of these tests revealed more than a most transitory increase in blood flow. Direct observations of the arteries in rabbits' ears showed a dilatation which lasted less than forty-eight hours. Injection of radio-opaque sodium iodide into the aorta of living animals by Moore, Williams, and Singleton (1933) showed no dilatation of the arterial tree in the leg after periarterial denervation, but a striking increase after lumbar ganglionectomy. Gilding (1932) has brought out the same effect by the intravenous injection of bromphenol blue during electrical stimulation of the stellate ganglion. On the stimulated side vasoconstriction was so intense that only a small quantity of dye reached the tissue, whereas in the opposite extremity they were deeply stained. On stimulation following periarterial sympathectomy there was no change in the straining reaction, but when a peripheral nerve was cut the vessels relaxed over an area identical to its peripheral distribution. Similar findings have been reported in man by Smithwick and White (1935), who observed that destruction of the peripheral nerves is followed by complete sympathetic paralysis throughout the denervated area.

Leriche (see *Nelson Loose-Leaf Living Surgery,* III, p. 788) himself was one of the first to recognize these objections and to base the physiological result of periarterial sympathectomy not on the direct interruption of vasoconstrictor nerves, but on the division of centripetal sensory fibers. But equally conclusive evidence has recently been presented against this hypothesis. Anatomically Stopford (1931) has been unable to prove the existence of ascending sensory fibers in the walls of blood vessels. By physiological investigation Moore and Singleton (1933) have studied the painful reactions that are produced by intra-arterial

injection of irritant solutions (lactic acid). The irritant reaction is not altered by arterial decortication or lumbar sympathectomy, but disappears after cutting the lumbosacral nerves peripheral to the origin of the sympathetic rami even when their sympathetic fibers are left intact. In human subjects Stürup and Carmichael (1935) tested the sensitivity of a digital artery in the little finger after anesthetizing the ulnar nerve in its epicondylar groove with procaine. Direct exposure and stimulation of the artery, both by a faradic current and by stretching and clamping, produced no sensory response. The nerve supply of the peripheral vessels is therefore quite different from that of the viscera.

To date no one has published any convincing demonstration of a durable increase in blood flow in human beings to offset evidence to the contrary in experimental animals. A rise in temperature of as much as 10 degrees may result for a week following any operation (Fig. 84). This is a non-specific effect due to destruction of tissue and the absorption of the resultant protein decomposition products. A similar, but more transitory, increase in circulation can be produced by the intravenous injection of a foreign protein, i.e., typhoid vaccine. We have seen the digital ulcerations of Raynaud's disease heal following this procedure. For the treatment of thromboangiitis obliterans or arteriosclerosis with painful gangrene of the foot, temporary interruption of the peripheral nerves gives both a greater and a more lasting increase in circulation than periarterial sympathectomy, and its effect on pain is likewise more complete (see Smithwick and White, 1935, and Chapter XXI).

From these considerations, as well as from many critical published case reports (see especially Demel, 1930, and Müller, 1928), and from experiences in this hospital with the periarterial operation in 24 patients (Allen, 1927), we have been forced to the conclusion that the only indication for periarterial sympathectomy lies in the rare case of traumatic arthritis with pain in the arm (Fontaine and Herrmann, 1933; see p. 236). Although fully convinced that the operation is often effective in this condition, it is questionable whether it has any specific effect. We would raise the question whether equally beneficial results cannot be obtained by paravertebral injection of the sympathetic ganglia or even by intravenous injection of typhoid vaccine.

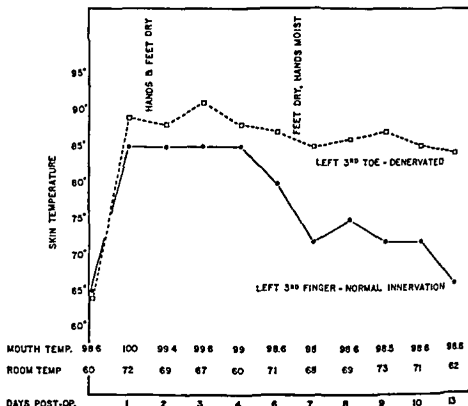


Fig. 84. The vasodilator effect which follows injury to the tissues after any operation.

In this instance bilateral lumbar ganglionectomy has caused a permanent increase in circulation to the feet. Note that during the first four days after operation the hands were equally warmed, and that this non-specific vasodilator response lasted for a week These measurements were made in this hospital by Dr Henry Heyl

Technic of Periarterial Sympathectomy. Leriche has given an excellent description of his technic for carrying out periarterial sympathectomy in *Nelson Loose-Leaf Living Surgery* (Vol. III, p. 780). After exposure of the selected artery under local anesthesia (the femoral in the lower part of Scarpa's triangle, the brachial in the mid upper arm), the common vascular sheath is opened and the artery freed from its venae comites and neighboring nerves. The adventitia of the artery is then picked up by a pair of fine-toothed forceps and incised longitudinally over a length of 5 cm. (Fig. 85B). Camera of Turin suggested the infiltration of normal saline under the adventitia to facilitate its separation from the media (Fig. 85A). This is an excellent procedure and, if procaine is substituted for saline, aids in the anesthesia. One of the lips of the incision is now grasped by a

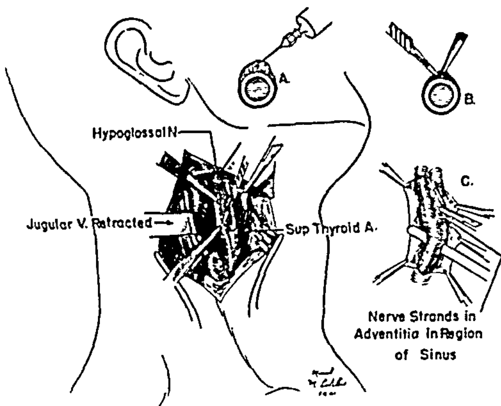


FIG. 85. Denervation of carotid sinus by decortication of common, external, and internal carotid arteries.

A. shows method of blowing the adventitia off the media by infiltrating procaine solution.
B. illustrates dissection of adventitia and its nerve fibers from media
C. The adventitia has been freed and the carotid body and the sinus nerves are being dissected from the region of the bifurcation.

number of fine hemostats and a blunt dissector used to detach the outer sheath (Fig. 85C). After both sides are freed, the artery is lifted up on a small ribbon retractor and the decortication completed posteriorly. Bleeding from the vasa vasorum is easily controlled by gauze pressure, but an occasional small arterial branch may require ligation. When all the adventitia that can be detached from the resistant plane of the media has been resected, the arterial wall becomes markedly contracted. This is a sign that a thorough decortication has been effected. The periarterial plexus can also be destroyed chemically, either by injecting alcohol beneath the adventitia (Handley, 1927) or by painting the outer coat of the artery with carbolic acid (Doppler, 1931).

Denervation of Carotid Sinus. Carotid sinus denervation involves a periarterial decortication of 2 cm. of the common carotid

artery below its bifurcation, and of the external and internal carotids for an equal distance above. Particular care must be exercised to insure a thorough removal of the filaments of the glossopharyngeal (sinus) nerve, and the vagal and sympathetic rami which enter the plexus between the origin of the two vessels.

In cases of an irritable sinus, deep ether anesthesia should be supplemented by local procaine block in order to prevent serious disturbances in pulse and blood pressure. Barbiturates such as evipal should never be used, as these compounds fail to decrease sinus irritability (Weese, 1939).* An incision centered on the hyoid bone is made along the anterior edge of the sternomastoid muscle, so that the muscle and jugular vein can be retracted posteriorly (Fig. 85). This gives easy access to the carotid artery, which is then separated from the underlying vagus and cervical sympathetic trunk well above and below the bifurcation. After this portion of the common carotid artery and its branches have been freed from neighboring structures it should be elevated from its bed by traction tapes. Beginning with the common carotid, the adventitial coat is blown off the media by infiltrating 1 per cent procaine solution between these layers. It is then a simple matter to dissect away the adventitia, although when there is a dilatation of the bulb with calcification of the media extreme care must be used to avoid a perforation. Stripping of the external and internal carotids is more difficult, because of the deep position of the internal carotid and the numerous branches of the external. Any of these may be ligated, if this facilitates a more thorough decortication. This is particularly true of the ascending pharyngeal artery, which leaves the main trunk right in the area of the carotid sinus. After its trunk has been ligated and cut away, a thorough dissection of this important reflex zone can be carried out. Only by thorough dissection over a wide area of at least 2 cm. above and below the bifurcation and of both the anterior and posterior surfaces can the surgeon make certain of securing the desired physiological effect and preventing regeneration.

* Our choice of an anesthetic is diametrically opposed to that of Rovenstine and Cullen (1939), who prefer the use of cyclopropane so that the surgeon can determine when the sinus has been thoroughly denervated by the cessation of reflex alterations in the pulse and blood pressure. We believe that this is unnecessary and dangerous

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Chapter XX

PARAVERTEBRAL INJECTION OF SYMPATHETIC RAMI AND GANGLIA

Paravertebral injection of the sympathetic rami and their ganglia constitutes a comparatively new and extremely valuable therapeutic as well as diagnostic procedure. We are indebted to Läwen (1923) for demonstrating the importance of procaine block in problems of diagnosis, to Brunn and Mandl (1924, 1925, and 1926) of Vienna for the application of this method to the relief of angina pectoris, and to Swetlow (1926) for introducing alcohol to obtain a lasting chemical block of the sympathetic fibers.

During the past fifteen years diagnostic and therapeutic injection has come into steadily increasing use. As has been stated in Chapter VII, the diagnostic value of paravertebral infiltration with procaine is great, because its temporary paralysis of sympathetic structures enables the surgeon to predict with accuracy the effect of their destruction on peripheral circulation and visceral pain. Furthermore, from the therapeutic point of view, repeated or even single infiltrations of anesthetic drugs may give lasting relief in traumatic arthritis, causalgia, and amputation stump neuralgia (see Chap. IX). In this clinic paravertebral alcohol injection has been used in preference to ganglionectomy only in individuals who are poor operative risks. This group is made up for the most part of cases of cardioaortic pain and advanced malignant disease. Nearly 100 patients have been submitted to this procedure. The majority have shown as complete and lasting an interruption of visceral pain as if the corresponding ganglia had been excised. In poor risk cases this method is much safer than surgical resection of the ganglia. The average patient is up and about on the day after injection, and one medical student, in whom the first and second

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the intercostal nerves, as they lie behind the ribs. For this reason it is not fair to expect paravertebral injection to relieve pain other than that transmitted over sympathetic pathways. Cardio-aortic pain, for example, can be permanently relieved, whereas pain in carcinoma of the lung, which involves the parietal pleura, is interrupted only as long as the intercostal nerves are paralyzed (a period of several weeks).

Articles Required for Injection. Needles should be 10 cm. long and constructed of rustless flexible steel. Thin lumbar puncture needles or the special Labat needles sold by the Anglo-French Drug Company in New York are most satisfactory. Each needle should be equipped with a depth marker to measure the distance it is to be pushed beneath the rib. A short length of narrow rubber tubing or a bit of bone wax serves this purpose well.

A hypodermic needle for making preliminary intracutaneous infiltrations of procaine at the points of insertion of the larger needles.

Any good 5 to 10 cc. glass syringe which fits the needles will serve for injection. It should have a smooth action plunger and be graduated in quarters or tenths of a cubic centimeter.

A metal centimeter rule.

Solution of 1 and 2 per cent procaine hydrochloride (in cases of coronary disease no adrenaline should be added).

Ninety-five per cent or absolute ethyl alcohol (C.P.).

A 1 cc. ampoule of lipiodol.

I. Paravertebral Injection of the Thoracic Sympathetic Rami and Ganglia *

In carrying out paravertebral injection of the upper thoracic ganglia, it is best to have the patient lying on his side, knees drawn up, shoulders at the edge of the bed, and head flexed forward, as though a high spinal puncture were to be performed. The head should be supported on a small pillow so that there will be no lateral curvature of the cervical spine. It is also important to arrange the patient so that he is not lying on his lower arm, and so that both hands are uncovered and can be ob-

* A large part of the following description and Figures 87 and 88 are taken from an article by White (1940). We wish to thank the publishers of *Surgery, Gynecology, and Obstetrics* for their kind authorization to reproduce this material.

thoracic ganglia were injected for hyperhidrosis, resumed his class work on the following morning.

Although these results as a whole are highly satisfactory, we must state most emphatically that there is no justification for the routine substitution of alcohol injection for ganglionectomy. In the first place, accurate injection is technically difficult even in thin-backed individuals. The injection must be made at a depth of from 5 to 8 cm. and within 5 mm. of the nerves to be destroyed. After a primary failure, secondary injections are rarely successful. For these reasons surgeons who are not willing to make a long, careful study of this method are certain to meet with disappointment. A second and more important objection to injection therapy, at least where the thoracic rami are concerned, is that it is frequently followed by an irritative neuritis. While the fine postganglionic sympathetic fibers may be permanently destroyed,* the neighboring heavily sheathed intercostal nerves undergo a very transitory paralysis. At the end of two to three weeks cutaneous anesthesia is usually replaced by hyperesthesia. Depending on the patient's psychic constitution, the resultant neuritis is likely to be more or less troublesome for a period of from one to three months. When ganglionectomy constitutes too great a risk, we do not consider the possibility of alcohol neuritis to be a serious objection. We do, however, believe that this possibility contraindicates the use of alcohol in the average patient.

In order to produce destruction of the spinal nerves, it is necessary to inject alcohol directly into their sheaths, a procedure which we have recommended for blocking the peripheral nerves in the lower leg (Smithwick and White, 1935). In paravertebral injection, however, the needles can rarely penetrate

* Merrick (1941) has recently investigated the effectiveness of alcohol in de-

with angina pectoris this may be a difficult matter. The points of injection are marked 4 cm. lateral to the spinous processes (Fig. 86). Following the use of tincture of iodine, acriflavine applied with a fine cotton applicator is an excellent marking

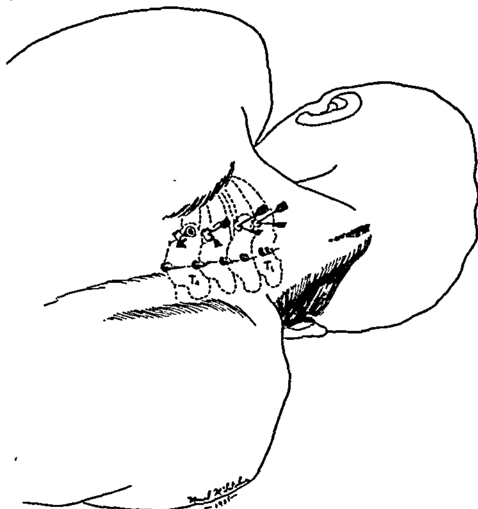


FIG. 86. Paravertebral injection of thoracic sympathetic ganglia: 1. Position of patient and bony landmarks for inserting needles.

(Reproduction from chapter by White in *Disease of the coronary arteries and cardiac pain*, edited by Robert L. Levy, Macmillan, 1936.)

medium, as the two substances combine to form a jet-black sterile mark.

The technic of inserting the needles is essentially Labat's (1924) second method of paravertebral injection. Procaine is injected intradermally 4 cm. lateral to the thoracic spines. Ten-

served for vasodilatation and paralysis of sweating. A final point of importance is that when alcohol is to be injected it is best to do the injection with the patient in his own bed. Complete immobility for an hour after injection allows the alcohol to become fixed in the tissues, whereas muscular movement on shifting a patient off the operating table tends to force the alcohol about in the retropleural tissues and thereby to cause pain and irritation of outlying nerves.

Injection of alcohol must be performed without a general anesthetic, because this masks the evidence of successful placement of the needles. The patient with angina pectoris must therefore be carefully medicated, in order to enable him to lie for an hour on his side with the minimal amount of discomfort and emotional strain. Having seen two patients die of coronary thrombosis a few hours before the time set for injection, and two others develop infarction during the procedure, we have become sensitized to the danger of psychic strain in persons with severe forms of angina pectoris. Patients are therefore routinely given 3 grains (0.2 gm.) of phenobarbital the evening before, and this is repeated once or twice in the morning before the bed is moved to the operating room. This usually insures a drowsy patient. In addition it has been shown by Weiss (1929) that the barbiturates reduce the chance of toxic reactions to procaine. It is also safer to administer 1/100 grain (0.6 mgm.) of atropine sulfate subcutaneously as a protection against syncope and other vagal reflexes. If on arrival in the operating room the patient is still restless and worried, an additional 1/6 to 1/4 grain (10 to 15 mgm.) of morphine should be given before inserting the needles. In any event, morphine should be available in a syringe for immediate subcutaneous injection in case the patient develops any severe pain during the course of the procedure.

The bony landmarks for paravertebral injection are the spinous processes. Due to their imbrication like the shingles on a roof, the tip of each marks the level of the transverse process and the posterior angle of the rib next below. Thus the highest prominent vertebral spine, the seventh cervical, marks the level of the first rib; this relationship holds over the entire length of the thoracic vertebrae. In thin individuals it is a very simple matter to locate the spines, but in the stocky type which so often goes

anterolateral surface of the vertebral bodies and looping over the heads of the ribs. The further forward the tips of the needles can be inserted and still maintain their contact with bone, the less alcohol will come in contact with the intercostal nerves and the greater amount will surround the gray visceral rami which run forward from the sympathetic trunk to the heart. A useful trick in working the tip of a needle forward alongside the vertebra is to start with the bevelled tip pointed medially. When bone is touched, the tip of the needle can often be made to scrape along it if the needle is rotated through 180 degrees so that its bevelled tip is turned away from the bone. A depth of even 4 cm. beneath the transverse process is quite safe, provided the tip of the needle still rests against bone, and injection of sclerosing solution at this depth is almost certain to destroy the visceral rami. An infiltration in this region will diffuse freely through the retropleural space, bathing the spinal nerves, the sympathetic trunk and its rami, and the cardiac nerves or splanchnic roots which run anteriorly into the posterior mediastinum (Fig. 88).

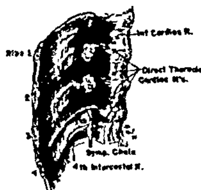


Fig. 88. Distribution of 2 cc. of methylene blue injected against the sides of the upper three thoracic vertebrae in a cadaver.

The dissection shows the way solutions diffuse in the retropleural plane around the sympathetic ganglia, communicant rami, cardiac, and intercostal nerves. (Reproduced from White, 1940, courtesy of *Surgery, Gynecology, and Obstetrics*.)

In performing these injections, the needles should never be attached to the syringe. Care should be taken that the tip of a needle does not lie within the pleural space, in a blood vessel, or in an outward prolongation of the subarachnoid space. None of these eventualities is dangerous provided it is recognized and the position of the needle corrected. With the tip touching bone, it is almost impossible for the solution to leak into the pleural cavity. Rapid aspiration of procaine placed in the butt of the needle, or a cough reflex on injection, indicates that the tip lies within the pleura. If it lies within a blood vessel or a lateral prolongation of the subarachnoid space, aspiration of blood or spinal fluid will make these complications obvious. Bloody taps are frequent under the upper two ribs, because the intercostal

centimeter needles (with depth markers on the shafts) are then inserted at these points and pushed inward perpendicularly to the skin until the transverse process or the articulating portion of the rib is touched at an average depth of from 2 to 5 cm. (Fig. 87, first position of needle). It is important to visualize the depth of the ribs in order not to penetrate the pleura and puncture the surface of the lung. If this happens, a spontaneous pneumothorax occasionally develops in the course of a few

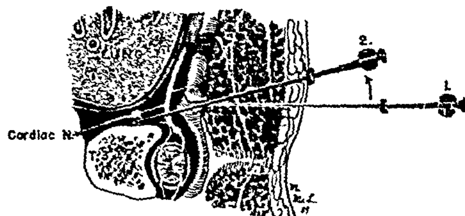


Fig 87. Paravertebral injection of thoracic sympathetic ganglia · 2. Insertion of needle for injection of cardiac nerves

1. Needle inserted 4 cm to left of spinous process and tip in contact with transverse process of vertebra. Depth marker has been set at a point 3 cm. from the skin 2. Shank of needle has been rotated outward and tip worked inward until at an additional depth of 3 cm it lies in contact with the side of the vertebra and in close approximation with the ganglionated sympathetic chain. (Reproduced from White, 1940, courtesy of *Surgery, Gynecology, and Obstetrics.*)

hours. Once contact has been made with bone, the tip of the needle is manipulated caudally until it touches the lower border of the transverse process. The depth marker is then pulled out to a distance of 4 cm. from the skin. Each needle is now inclined to an angle of approximately 20 degrees with the median sagittal plane and perpendicular to the curvature of the back in relation to the long axis of the thorax. When thrust inward on this bearing a second contact is usually made with bone at a further depth of 3 cm. (Fig. 87, second position of needle). If sooner, the needle must be withdrawn and reinserted at a slightly lesser angle. On the other hand, if no contact is made at 3 cm., the needle must be directed further toward the midline. The paravertebral ganglionated chains lie at an average depth of 3 cm. beneath the transverse processes, running along the

anterolateral surface of the vertebral bodies and looping over the heads of the ribs. The further forward the tips of the needles can be inserted and still maintain their contact with bone, the less alcohol will come in contact with the intercostal nerves and the greater amount will surround the gray visceral rami which run forward from the sympathetic trunk to the heart. A useful trick in working the tip of a needle forward alongside the vertebra is to start with the bevelled tip pointed medially. When bone is touched, the tip of the needle can often be made to scrape along it if the needle is rotated through 180 degrees so that its bevelled tip is turned away from the bone. A depth of even 4 cm. beneath the transverse process is quite safe, provided the tip of the needle still rests against bone, and injection of sclerosing solution at this depth is almost certain to destroy the visceral rami. An infiltration in this region will diffuse freely through the retropleural space, bathing the spinal nerves, the sympathetic trunk and its rami, and the cardiac nerves or splanchnic roots which run anteriorly into the posterior mediastinum (Fig. 88).

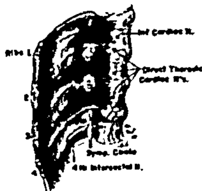


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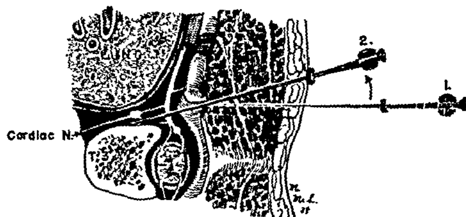


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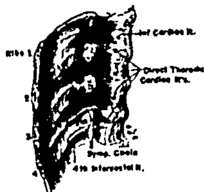


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The dissection shows the way solutions diffuse in the retropleural plane around the sympathetic ganglia, communicant rami, cardiac, and intercostal nerves. (Reproduced from White, 1940, courtesy of *Surgery, Gynecology, and Obstetrics*.)

In performing these injections, the needles should never be attached to the syringe. Care should be taken that the tip of a needle does not lie within the pleural space, in a blood vessel, or in an outward prolongation of the subarachnoid space. None of these eventualities is dangerous provided it is recognized and the position of the needle corrected. With the tip touching bone, it is almost impossible for the solution to leak into the pleural cavity. Rapid aspiration of procaine placed in the butt of the needle, or a cough reflex on injection, indicates that the tip lies within the pleura. If it lies within a blood vessel or a lateral prolongation of the subarachnoid space, aspiration of blood or spinal fluid will make these complications obvious. Bloody taps are frequent under the upper two ribs, because the intercostal

branch of the costocervical artery parallels the first and second thoracic ganglia. Spinal fluid is more rarely aspirated, but the possibility of a high spinal injection of either procaine or alcohol is a serious matter. This is most likely to happen if the needle is passed over the upper border of a rib in a cephalad direction. We have withdrawn spinal fluid twice, and know of three instances of intrathecal injection of either procaine or alcohol. When all of the needles have been properly placed they should form a characteristic pattern with their shafts lying in the same sagittal plane. In injecting the cardiac plexus (T_1-T_4) the uppermost needle should be inserted deepest and point in a slightly more caudal direction than the others. In diagnostic block, 5 cc. of 1 per cent procaine adrenaline solution is slowly injected through each needle.

In order to inject alcohol and produce a lasting chemical destruction of the visceral nerves a special technic has been developed. In cases of cardioaortic pain,* 2 cc. of 2 per cent procaine solution without adrenaline is first injected through each needle. If properly placed, this minimal amount of solution produces clear-cut signs of intercostal and sympathetic nerve paralysis within a period of five to ten minutes. Anesthesia appears in the axilla and over the third and fourth ribs front and back. No anesthesia develops over the first and second ribs, as this area is also innervated by descending branches of the third and fourth cervical nerves. No anesthesia should develop in the arm or hand, but this entire region, as well as the side of the neck and face, should become hot and dry. This unilateral sympathetic paralysis is particularly striking when the hands are cold or sweaty from nervousness. Horner's syndrome is a less useful sign, as it is often hard to make out with the patient lying on his side and with the pupils constricted after morphine. When these signs appear rapidly it is good evidence that the needle tips lie close to the sympathetic trunk. If they fail to develop within ten minutes, it is best to withdraw the needles and reinsert them at a later time. It must be borne in mind that procaine diffuses through the tissues far more readily than alcohol, and experience has shown that unless a clear-cut block can be

* The procedure described below is for use in angina pectoris, as it is used most frequently for this purpose The procedure for injecting the lower thoracic ganglia and splanchnic rami is essentially the same

produced by a minimal quantity there is no assurance of a lasting paralysis with 5 cc. of alcohol.*

When satisfied that the needles have been placed correctly and that there is no anesthesia of the ulnar nerve or evidence of subarachnoid block, it is advisable to inject a further 3 cc. of 1 per cent procaine into each. This supplementary infiltration is to insure a widespread anesthesia, so that the final injection of alcohol will be painless. The additional dilution of the alcohol does not seem to prevent an effective destruction of nerve tissue.

The final injection of 95 per cent alcohol is carried out very slowly, injecting a total of 5 cc. into each needle, but drawing back on the plunger after each half cubic centimeter has run in to make sure that the needle tip cannot have shifted and penetrated a blood vessel or the subarachnoid space. Several minutes should be spent in injecting the alcohol through each needle. If the patient complains of any undue discomfort, the injection must be stopped for a few minutes until the pain subsides. By following the alcohol with a few drops of lipiodol, the exact location of each needle can be identified by subsequent anterior-posterior and lateral spinal x-rays (Fig. 55). This is of great value in developing the technical skill of the operator and in discovering the cause of failures. Often it is found that the highest point of injection is alongside the second thoracic vertebra, but the nerves at the side of the first are also most important. In the thick-backed individual it is often difficult to identify the first rib. As it is most undesirable to inject alcohol above it in the region of the brachial plexus, one is often forced to play safe and select the lower of two doubtful points. On several occasions when anginal attacks have persisted in the arm and under the upper sternum, subsequent x-rays have shown no lipiodol above the second thoracic vertebra. This residual pain has disappeared after a more accurate injection under the first rib made possible by x-ray localization.

After the needles have been withdrawn, the patient should be kept on his side with his back supported by a pillow and as quiet as possible for an hour or more in order to minimize diffusion of the alcohol. He may then be shifted over onto his back, and

* Five cc. of alcohol injected into the thigh muscle of a rabbit causes an area of necrosis little over 1 cm. in diameter.

after two hours allowed to assume any desired position in bed. Most patients can be up on the following day and leave the hospital within seventy-two hours.

Complications. At the Massachusetts General Hospital early post-injection complications in a series of over 100 injections have been limited to:

a. One case of severe pleuritic pain, which required large doses of morphine and lasted six hours. This was probably due to some alcohol leaking into the pleural cavity.

b. Several cases of transitory mild pleuritic pain, which developed a few hours after injection as the procaine was absorbed. This required chest strapping and morphine in several instances, but in all but one patient it disappeared overnight.

c. One case of pneumonia which occurred in a woman of 85 dying of coronary infarction. Alcohol was injected to relieve intractable pain.

d. Three cases of pneumothorax, which were caused by a needle perforating the pleura and causing slow leaks of air from injured alveoli. One of these required subsequent aspiration of the air.

Although no instance of intrathecal injection has occurred in this series, such an accident has been reported by Molitch and Wilson (1931) and resulted in a Brown-Séquard paralysis, which fortunately cleared up. Precautions which can be taken to avoid this most serious complication are: Never slide the needle over the upper border of a rib in a cephalad direction; always insert *the needle detached from the syringe, and draw back on the* plunger at frequent intervals during the actual injection. In spite of these precautions, a colleague has informed us that he has produced a high spinal anesthesia in the course of his preliminary procaine injection. However, if a volume of only 2 cc. of 2 per cent solution is used as a test for the position of each needle, the risk of injecting this small amount (40 mgm.) is practically negligible.

Late complications have consisted of intercostal irritation and neuritis. The sympathetic ganglia lie so close to the intercostal nerves that alcohol infiltrated around the chain cannot help bathing their trunks. They are paralyzed at first, but anesthesia begins to disappear in their anterior divisions within a fortnight. Within a month the intercostal nerves are recovering along their entire length, and with this there is a greater or lesser degree

of hyperesthesia of the chest wall, which commonly persists for a number of months. Most patients state that pressure of clothing irritates the tender skin, and that there is a burning sensation with occasional shooting pains. In most cases the discomfort is quite bearable and clears up in a month or two. In others (about 10 per cent) it is most troublesome and requires mild sedation with acetyl salicylic acid or empirin compound, phenobarbital at night, and occasional doses of codeine. Baking the hypersensitive areas is often a great help. With the exception of a neurotic woman and one other individual in whom the injection failed to relieve the anginal attacks, all the patients have stated that they would willingly submit to a second injection if their pain should ever recur.

There is no question that neuritis constitutes a serious objection to treatment by alcohol injection. In advanced coronary and malignant disease its disadvantages are far less than the risk of mortality from operation, but it limits the application of the method to the severer cases.

Duration of Sympathetic Paralysis. While alcohol causes only a transitory paralysis of the heavily sheathed intercostal nerves, it most frequently produces a permanent interruption of the afferent pathways of visceral pain. We have 1 patient under observation who has had relief of attacks of angina pectoris in the left precordium and arm for over eight years, and 14 others without recurrence for over two years. Another patient with an intensely painful aortic aneurysm was relieved of pain for five years. In the attempt to secure a permanent vasomotor paralysis we have been less successful. A few of these individuals have shown as satisfactory results at the end of a year as after the average cervicothoracic ganglionectomy, but more frequently there has been a recurrence of sympathetic motor function at the end of six months. These findings are in agreement with results published from other clinics (Flothow, 1931; Reichert, 1933).

II. Paravertebral Injection of the Lumbar Sympathetic Rami and Ganglia

In lumbar as in thoracic paravertebral injection, the spinous processes constitute the important bony landmarks. A transverse line drawn tangent to the upper edge of the spinous process of any lumbar vertebra marks the level of its transverse proc-

ess. Unlike the thoracic spines, which point obliquely downward and are imbricated one over the other, the lumbar spinous processes are separate vertical blades of bone which project 2 to 3 cm. above the vertebral lamina. Except in unusually stout patients, their tips are easily palpated, and measure from 1.5 to 2.5 cm. in length and about 5 mm. in thickness. There is a

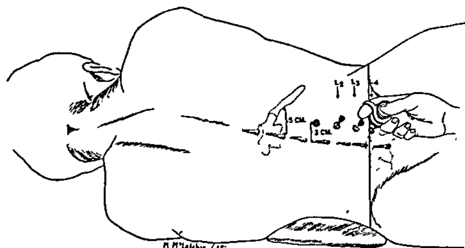


FIG. 89. Paravertebral injection of lumbar sympathetic ganglia: 1. Bony landmarks for inserting needles.

well marked depression about 0.5 cm. long between each pair of lumbar spines. The method of identifying the individual processes is shown in Fig. 89.

Injection can be made with the patient lying flat on his stomach or turned on the side opposite the one to be injected. In the technic described by Labat (1924) needles 8 to 10 cm. in length are inserted through the skin 3 cm. lateral to the upper edge of each lumbar spine. When pushed perpendicularly inward to a depth of 3 to 4 cm. they should make contact with the transverse process of the same vertebra. If bone is not felt at this depth, the direction of the needle must be slightly altered, either upward or downward. After the transverse process has been located, the needle is pointed slightly upward to pass above the transverse process and inward at a slight angle toward the midline. It is then thrust slowly down through the psoas muscle until its tip can be felt scraping along the edge of the vertebra.*

* As the lumbar nerves lie midway between the transverse processes, the needles must be advanced slowly and their direction changed if paresthesias are produced.

(Fig. 90). A rubber marker is of great assistance in measuring the correct depth. Injection made against the sides of the vertebrae and 2.5 to 3.5 cm. beneath their transverse processes will result in a thorough blocking of the sympathetic rami and the

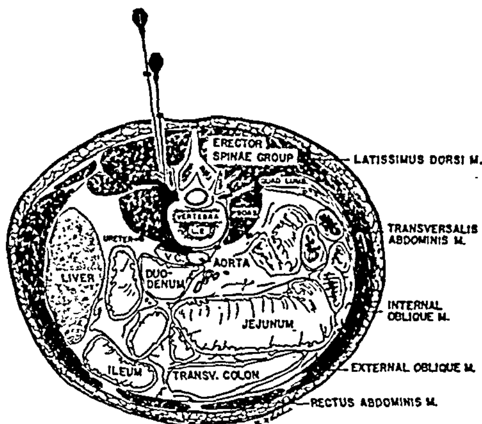


Fig. 90. Paravertebral injection of lumbar sympathetic ganglia. 2. Method of inserting needles.

corresponding ganglia, with little if any infiltration of the lumbar nerves.

In order to block the second to fourth lumbar ganglia, we have inserted needles above the three lower lumbar transverse processes. As in the thoracic region, it is important to insert the needles separate from the syringe, to place their tips against the bony sides of the vertebrae, and then to aspirate each in turn before injection. By observing these precautions the danger of injecting procaine or alcohol into a blood vessel or the subarachnoid space can be averted. Procaine-adrenaline solution should then be injected through each needle. The rapid warming and drying of the corresponding foot is proof that the needles

are accurately placed. With such a deep injection there is commonly only partial anesthesia of the skin in the back, the side of the buttock, and over the distribution of the genito-femoral, anterior femoral, and lateral femoral cutaneous nerves.

If alcohol is to be injected to obtain a lasting block, only a small amount of procaine (2.5 cc.) should be injected at first to make sure that the needles are in close approximation to the sympathetic trunks on the anterolateral surface of the vertebral bodies. Then if signs of sympathetic paralysis fail to develop, it is best not to attempt any readjustment of the needles or further infiltration of anesthetic solution, because of the danger that larger quantities of procaine will paralyze nerves beyond the zone which can be destroyed by alcohol. Under these circumstances it is advisable to give up for the moment and attempt the injection again at a later date.

After the needles are accurately placed, another 3 cc. of 1 per cent procaine should be infiltrated through each in order to insure thorough anesthetization of the tissues; this should be followed by 4 to 5 cc. of 95 per cent alcohol. If this is run in at a very slow rate and interrupted for a few minutes on the slightest sign of pain, it is usually possible to carry out the injection with very little discomfort to the patient. Injection of 0.25 cc. of lipiodol before withdrawing the needles enables a valuable x-ray check to be made on the position of the alcohol. After injection the patient should be kept quiet for several hours to prevent diffusion of the alcohol by muscular movements. There is, however, no need to keep him in bed on the following morning nor in the hospital for more than two or three days.

Complications. Neuritis is rare after lumbar paravertebral injection, because the alcohol is injected a full 3 cm. in front of the lumbar nerves and is separated from them by the psoas muscle. Our only complications have been transitory psoas weakness and a bedsore in an early case. In this instance a patient who was relieved of unbearable pain from embolism of the common iliac artery developed extensive anesthesia of the buttock. This complication can usually be avoided if cutaneous anesthesia is searched for and care taken to keep the patient's weight off the insensitive area. As sensory loss rarely lasts beyond a few weeks and there is no need to keep the ordinary patient in bed, this is not usually a difficult matter.

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Chapter XXI

PERIPHERAL SYMPATHECTOMY BY CRUSHING THE MIXED NERVES IN THE LOWER EXTREMITY

This procedure was developed to relieve the severe rest pain which is often a major problem in the management of certain cases of thromboangiitis obliterans and arteriosclerosis. In the presence of localized ulceration or gangrene of the toes or more distal portions of the foot, these patients often suffer untold agony. Our primary purpose was to render such areas insensitive so that antiseptic dressings could be tolerated. This not infrequently resulted in healing as well as improvement in the general condition of the patients. They then were able to sleep without drugs, and cooperate in other forms of conservative treatment designed to improve collateral circulation.

In many instances, a substantial and persistent rise in surface temperature of the denervated area was noted. Such a response is shown in Figure 91. It therefore became apparent that an actual increase in peripheral blood flow had resulted from interruption of vasomotor pathways which accompany the crushed sensory nerves. The beneficial effect of this procedure depends in part, therefore, upon this peripheral form of sympathectomy. While lumbar sympathectomy will cause a similar and perhaps greater increase in circulation, it has not been effective in relieving the pain of ulceration and gangrene. Those cases which do show an increase in blood supply to the part after nerve crushing should, in our opinion, be sympathectomized before the nerves regenerate, provided healing of the ulcerated or gangrenous areas is taking place. Furthermore, all stiff, scarred, useless toes which remain should be removed through the base of the proximal phalanges using lateral skin flaps. This type of closed amputation can be done with safety in the absence of

main vessel pulsation provided the technic is beyond reproach, all ulceration has healed, and an adequate collateral circulation has developed. *To leave these superfluous toes behind is only* courting future episodes of ulceration or gangrene, as lesions of this type nearly always commence in a digit. Our best results in cases having these severe forms of obliterative vascular dis-

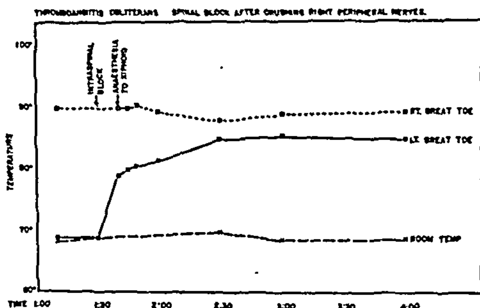


Fig. 91. Vasodilatation after crushing peripheral nerves.

Crushing the peripheral nerves resulted in a marked vasodilator response. Previous to crushing the posterior tibial, superficial, and deep peroneal nerves ten days before, the skin temperature of both great toes was the same. The denervated great toe on the right is now 20 degrees warmer and fails to rise any further after *high spinal anesthesia*, whereas the left great toe shows a typical vasodilator response.

ease have followed the judicious use of peripheral nerve crushing, sympathectomy, and minor amputation of useless digits. These operative procedures have been combined with other conservative forms of treatment such as vascular exercises, careful hygiene, and elimination of the use of tobacco. The results, as judged by the incidence of major amputations, in cases grouped according to main vessel pulsation are given in Chapter VIII, Tables V, VI, and VII.

Alcohol injection of the posterior tibial nerve was performed by Silbert (1922) for relief of pain in thromboangiitis. An incision was made at the level of the internal malleolus, exposing the nerve and injecting alcohol under direct vision. Some diffi-

culty with wound healing was encountered. It seemed to us that all of the five nerves concerned could be exposed at higher levels in the leg. By selecting the proper combination of nerves it was found possible to relieve pain completely and to practically eliminate the incidence of poor wound healing without sacrificing important motor fibers to the muscles of the lower leg. After considerable experience with this method we found that crushing of the nerves was easier and more satisfactory than their injection with alcohol.

The neuroanatomy of the lower leg and the technic of operation have been described in detail by Smithwick and White (1930 and 1935). The positions of the five nerves which transmit sensation from the foot are shown in Figure 92. It may be necessary to block one or all of these nerves in a given case. This should be done at a point sufficiently high to include all collateral branches which reach the painful zone, but at the same time below the motor branches to the important muscles in the leg. In general the optimum point to accomplish this is at the junction of the middle and lower thirds of the leg (about six inches above the ankle). Experience with many patients has shown that small, longitudinal incisions at this level in cases of thromboangiitis obliterans will nearly always heal, provided the gangrene is confined to the anterior part of the foot. First intention healing has taken place even in the absence of any peripheral pulsations in Buerger's disease, but in arteriosclerosis this cannot always be counted on when the popliteal artery is occluded.

In order to insure healing in legs with a poor blood supply, operations should be performed with meticulous care against trauma and sepsis. Forceps should not be used on the skin; retraction should be very gentle. It is essential to know exactly where the nerves lie (Fig. 92), so that lateral dissection and stretching of the tissues can be avoided. On the rare occasions when bleeding vessels are encountered, only the finest chromic catgut ligatures (0000) should be used. To avoid further foreign material in the wound, it is best not to suture the fascia; the skin should be loosely sutured with the finest silk. As a general rule only *one nerve, or at most two nerves, should be exposed at a time.*

Experience has shown that the simplest way to paralyze a

nerve so that it can be counted on to regenerate is to crush it in a hemostat. A nerve so treated over an extent of 3 to 5 mm. at the junction of the middle and lower thirds of the leg will regenerate in about three to six months. Crushing the nerves has numerous advantages over alcohol injection, which was previously recommended by us. Smaller incisions are possible, chemical irritation of the tissues is avoided, and the period of nerve regeneration is easier to control. We do not favor section

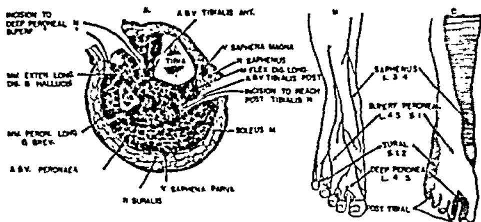


Fig. 92. Technic of exposing the mixed nerves in the lower leg. (Adapted from John Homans' *Textbook of Surgery*, 1932, courtesy of Charles C. Thomas)

and resuture of the nerves, as recommended by Laskey and Silbert (1933), as this is no more effective than simple crushing and makes the operation more complicated and difficult.

This minor procedure, when properly carried out, causes virtually no discomfort or subsequent inconvenience to the patient. He can be up in a chair after his return to the ward. The relief of pain and freedom from vasoconstriction are an enormous advantage in treating patients with thromboangiitis obliterans. The temporary motor and sensory paralysis resulting from this procedure has no serious untoward effect. Patients walk surprisingly well when the intrinsic muscles of the foot are paralyzed. Care should be taken to see that shoes fit properly to avoid ulceration from pressure. Patients should be cautioned against use of excessive heat. One patient received a severe burn from resting his denervated foot upon a hot radiator. The sensory nerves regenerate very completely. Some atrophy of the intrinsic muscles of the foot may persist but has not been trou-

blesome. The operation should not be used as a treatment for vasospastic disorders. It is intended only as a means of tiding the patient over a critical period of ulceration and gangrene. It is difficult to state the results with accuracy because other forms of treatment are used as well in most of these patients. Our impression, however, is that this operation has doubled the number of successful minor amputations of ulcerated or gangrenous toes, and has reduced major amputations to one-third of the number which was necessary before its introduction.

The principle of this operation can be applied to the upper extremity, although the need for crushing the nerves to the hand rarely arises. We have successfully denervated painful ulcerated or gangrenous digits in the upper extremities by crushing the sensory nerves concerned. Those to the dorsum of the hand can be crushed at the wrist. The digital branches of the ulnar and median nerves can be exposed distal to their important motor outflow through small longitudinal incisions in the palm.

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